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Measurement of Benzene Body-Burden for Populations Potentially Exposed to Benzene in the Environment

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A pilot study was performed to assess the measurement of benzene body-burden for populations potentially environmentally exposed to benzene. Probability sampling was used to select the participants in the two study geographical sites, Harris County, TX and St. Louis, MO plus parts of Wood River, Roxana, South Roxana and Hartford, IL.

Benzene levels were measured for the air and water environmental exposure for each participant and the benzene body-burden was measured through breath levels and, in a subsample, blood levels.

A pretest of occupationally exposed and non-exposed individuals was used to test analytical methodology and the concept of breath as an indicator of body-burden. The blood benzene levels expected and observed required analytical methods capable of measuring - 1 μg/L or below. This methodology did not exist and had to be developed for the pretest and pilot study. Benzene levels for smokers and non-smokers were compared in the pretest.

The range of air benzene levels found in the Harris County study (49 participants) was 2 to 45 $\mu g/m^3$ with a weighted means of 16.1 $\mu g/m^3$; breath levels ranged from 0 to 14 $\mu g/m^3$ with a weighted mean of 2.9 $\mu g/m^3$. In the St. Louis (68 participants) study the range of air benzene levels was 3 to 125 $\mu g/m^3$ with a weighted mean of 26.8 $\mu g/m^3$; breath levels ranged from 1 to 26 $\mu g/m^3$ with a weighted mean of 8.5 $\mu g/m^3$.

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A pilot study was performed to assess the measurement of benzene body-burden for populations potentially exposed environmentally to benzene. Probability sampling was used to select the participants in the two geographical sites, (1) Harris County, TX, and (2) St. Louis County, MO, parts of Wood River, Roxana, South Roxana, and Hartford, IL.

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SECTION 1

INTRODUCTION

Benzene is not only a fundamental and well-known organic chemical, it is also a chemical of major industrial importance. In the United States, benzene ranks 13th in volume (1) with a production for 1976 of 1.5×10^9 gal (2). Most (88%) of the domestic benzene production is from petroleum sources with the remainder from coal (3). The largest benzene source is the catalytic reforming process at oil refineries. Other major production routes are dealkylation of toluene and coproduction, with ethylene, from steam crackers (2).

The primary uses of benzene are chemical manufacturing, solvent operations, and as an additive in gasoline. Chemical processing is the major use. Although benzene is used in the commercial production of literally hundreds of compounds (4), its major uses are as the starting material for styrene (45%), cumene/phenol (20%), and cyclohexane (17%) (2). These compounds, in turn, are used in production of polystyrene plastics and rubbers and other fabricated plastic products. Despite its widespread industrial use, more of the population is exposed to benzene from the use of automobiles than from all other uses combined. This includes benzene exposure from gasoline service stations and from general automobile exhaust (5).

Although benzene is widespread in the environment, the levels of environmental exposure are significantly less than the levels of industrial exposure. Risk assessment is hampered by the lack of reliable dose response toxicity data, especially in humans. Therefore, the health consequences at ambient benzene concentrations are speculative.

The health effects of benzene have been reviewed extensively recently (6), especially with respect to its potential carcinogenic effects. Eventhough benzene toxicity has been recognized for over 50 years, much of its action is still poorly understood. It is clear that the most serious effect of chronic exposure is depression of the hematopoietic system, ranging from mild reversible depression of some of the formed elements to aplastic anemia and leukemia. The latter has been particularly difficult to study since no animal model has been found in which benzene induces leukemia despite epidemiological evidence linking the two in humans. Other toxic effects of benzene are central nervous system depression, and histochemical changes in kidney, liver, small intestine, spinal cord, and heart (7).

In view of these serious consequences from chronic benzene exposure, an evaluation of the exposure/body-burden of benzene in the general human population in areas of relatively high (industrial and urban), medium (urban), and low (rural) exposure was undertaken. Relatively little was known at the project's initiation about benzene levels in ambient air and especially about measurement techniques for assessing body-burden at very low benzene levels. Blood and breath levels had been measured (8) after 25-ppm exposure for 2 hr. The extrapolation of these data to exposures of 1 to 40 ppb indicated that new and innovative sampling and chemical analysis techniques would have to be developed to accomplish the objectives of the study, i.e., to measure benzene body-burden at ambient benzene exposures.

To test the methodology that was developed, a pretest was performed using nine individuals both occupationally exposed to benzene and nonoccupationally exposed. This pretest included smokers as well as nonsmokers. A semiportable spirometer (Figure B-1) was developed that permitted the collection of breath samples, and analytical methods capable of detecting benzene in blood at 1 ng/mL were developed. This technology was evaluated on the pretest subjects.

Using the information derived from the pretest, and air monitoring data that became available, two sites were selected for study: (1) Harris County, TX (Houston), and (2) St. Louis County, MO, with parts of the municipalities of Wood River, Roxana and Hartford, IL, included (St. Louis).

A team of RTI specialists was brought together for the execution of these studies. A diagram of the responsibilities of each center or division is given in Table 1.

The Sampling Research and Design Center (SRDC) devised the survey design used. The sampling frame was constructed and the areas designated for counting and listing of housing units. The sampling frame information and maps were transmitted to Survey Operations Center (SOC) staff who executed the counting and listing of housing units. SRDC then selected housing units to be screened for eligibility and willingness to participate. A random sample was selected by SRDC from the eligible individuals identified during screening. SOC staff then arranged for the actual sample collection (breath and air) by Analytical Sciences Division personnel. In addition, SOC personnel administered the study questionnaire and collected tapwater. If blood collection was scheduled for the participant, SOC arranged for a phlebotomist to collect the sample.

Analytical Sciences Division (ASD) staff, in addition to collecting the air and breath samples, maintained custody of all other samples and provided for their transport to the laboratory. All of the benzene determinations in each medium were performed by ASD and the data were supplied to the Statistical Methodology and Analysis Center (SMAC) for analysis. The sampling weights, study questionnaire, and chemical determinations were also analyzed by SMAC.

One of the significant contributions of this program was the integration of sampling design, field operations, chemical sampling and analysis, and

Table 1. ORGANIZATION AND RESPONSIBILITIES OF THE CENTERS AND DIVISIONS PARTICIPATING IN THE STUDY

Sampling Research and Design Center (SRDC)	Survey Operations Center (SOC)	Analytical Sciences Division (ASD)	Statistical Methodology and Analysis Center (SMAC)
• Designed survey and sampling frame • Drew the sample • Assigned sampling weights	• Coordinated all field activities • Counted and listed housing units in areas designed in the sampling frame • Conducted the household screen for eligible and willing participants • Scheduled appointments for air monitoring and breath and blood collection in coordination with ASD staff • Administered the study questionnaire to participants • Collected tapwater samples and arranged for a phlebotomist to collect blood samples	• Coordinated with SRDC and SOC all activities • Developed analytical and chemical sampling techniques for the study • Tested methods in pretest • Collected air and breath samples • Analyzed air, breath, blood, and water samples for benzene	• Analyzed the chemical data from ASD • Analyzed the questionnaire data from SOC • Applied the sampling weights from SRDC

statistical data analysis with experts in each of these fields performing their respective roles.

SECTION 2

RESULTS AND CONCLUSIONS

Sample collection and chemical analysis methods were developed and/or improved in order to execute this study. The pretest was performed to validate the chemical sampling and analysis methods developed. Nine individuals participated, including smokers and nonsmokers and occupationally exposed and nonexposed individuals. As a result of this pretest, a spirometer for collection of breath samples and analytical methods capable of detecting benzene in blood at 1 ng/mL were developed.

The execution of this study required clearance by the Office of Management and Budget (OMB) under the Federal Reports Act because a questionnaire was to be administered to the human subjects. Approval was granted with the understanding that:

1. "These surveys are being conducted as a pre-test of the feasibility of the information collection procedures;
2. That the information collected will not be used to generalize to either local areas or the nation as a whole."

In deference to these stipulations, only conclusions about the methods used will be made and the studies conducted in Houston, and St. Louis, will be referred to as pilot studies.

The survey had a two-stage design with stratification imposed at the first stage. First-stage sampling units were clusters of housing units, called segments, from which a sample of eligible persons was selected for the second stage of sampling. The degree of stratification of the exposure areas had strong implications on the level of effort required to collect the air and body-burden samples. In the Harris County, TX, pilot study, 15 first-stage strata were used. The distances between sampling points were great and sample collection was slow. In the St. Louis, MO-Wood River/Roxana/Hartford, IL, pilot study, 9 first-stage strata were used and the level of effort to collect samples from a greater number of participants was reduced by about one-third.

Of the exposure and body-burden samples evaluated, only air and breath showed detectable benzene levels in the majority of samples for environmentally exposed individuals. In the other two matrices, water and blood, benzene was at or near the detection limit for all samples. Hence, water and blood samples do not appear to be good indicators of either exposure or body-burden at environmental levels. To compound the problem of low level exposure/body-burden, benzene is ubiquitous in ambient air. Its presence in all air samples limits the lower end of the dynamic range. The differentiation must then be made between population body-burdens differing by factors of 2 or less instead of by orders of magnitude as might be expected with some pollutants.

The range of air benzene levels in the Harris County study was 2 to 45 $\mu g/m^3$ with a weighted mean of 16.1 $\mu g/m^3$; breath levels ranged from 0 to 14 $\mu g/m^3$ with a weighted mean of 2.9 $\mu g/m^3$. In the St. Louis study the range of air benzene levels was 3 to 125 $\mu g/m^3$ with a weighted mean of 26.8 $\mu g/m^3$; breath levels ranged from 1 to 26 $\mu g/m^3$ with a weighted mean of 8.5 $\mu g/m^3$.

SECTION 3

RECOMMENDATIONS

Further study in the area of exposure and body-burden should include a wider activity range of the participants. Personal monitors should be attached to the participant to accurately assess their exposure during outdoor activities. Ambient air benzene levels have been recorded in the St. Louis, MO-Wood River/Roxana/Hartford, IL, study area that were a factor of 2 above the highest air level found in this study (9).

Retesting of participants would provide better information concerning individual variation and response to variations in exposure. The additional burden on the participant would require careful consideration, however.

Several recommendations concerning the field procedures have developed from discussions at RTI and with the field staff. The first concerns the timing of the study. The break between screening and final sample enrollment should be made as short as possible, since people's health and activity patterns change and a person screened as eligible may no longer be so at the time of actual sampling. The shorter the time interval, the less likely the change.

The second area of concern is the size and location of the areas being sampled and the size of the field staff. It is vital once the sample frame is developed and the participants screened and selected that the activities of the field staff be examined in terms of time and distance between areas and that the size, composition, and schedule of the field study staff be determined accordingly. Careful scheduling of activities can alleviate problems to some extent. However, the outcome of the study will depend on the ability of the field team to cover all areas and all persons within the time scheduled.

Analytical methods capable of detecting benzene in blood at 0.05 μg/L or less need to be developed to evaluate blood as an indicator of benzene body-burden. Examples of such methods are photoionization detection optimized for benzene and use of on-line headspace purge and cryogenic focusing prior to gas chromatography.

Any study of this general scope should not be undertaken without a full complement of experts in sampling design, survey operations, chemical sampling and analysis, and design and statistical analysis. Inexperience in any of these areas may lead to errors that could invalidate or bias the entire study. Each of these areas is essential to the design, execution, and interpretation of studies relating to environmental exposure and body-burden.

SECTION 4

EXPOSURE OF POPULATIONS TO BENZENE

BENZENE MANUFACTURING SITES AND INDUSTRIAL USERS

The benzene production capacities are listed by state in Table 2 for petroleum-based benzene and in Table 3 for coal-derived benzene (3,10). These facilities are highly concentrated in the Texas Gulf Coast region, with several in the Northeast, and others scattered nationwide.

The most extensive industrial use of benzene is as a starting material for the production of other chemicals. Table 4 lists the benzene user facilities, their location, and their processes (5). Again, the geographical distribution is the same--high concentration of benzene utilization in the Gulf Coast area, less in the Northeast, and a scattering of facilities nationwide.

EMISSIONS AND AMBIENT MONITORING DATA

Because of its volatility, benzene is undoubtedly released to the environment at many steps of production, storage, transportation, and use. Petroleum refining accounts for approximately 27×10^6 kg/yr of total benzene emissions. Approximately 4×10^6 kg/yr of benzene is emitted by solvent operations. Estimates of benzene emissions from several of the major by-product manufacturing operations are given in Table 5 (5). An upper limit was estimated using a material balance and all losses were assumed to be benzene, although certain processes are multistep and the material lost may not be benzene. The lower limit was obtained from estimates of the losses based on the processes with the applicable control technology.

Emissions estimates are useful for predicting where ambient air levels may be high; however, they are no substitute for air monitoring. For example, the Houston, TX, area would appear to be a potentially benzene-contaminated area because of the industrial activity. A study by the Texas Air Control Board (11) in Houston, TX, of ambient air benzene levels showed levels that ranged from 2.2 to 30 ppb. To differentiate between benzene derived from combustion processes (auto exhaust) and that from industrial sources, acetylene, another combustion product, was monitored simultaneously. The results were ratioed and the ratio and absolute values were correlated with wind direction. The results were used to identify components of the ambient benzene levels due to traffic patterns and industrial activity on the Houston ship channel.

Table 2. PETROLEUM REFINERIES PRODUCING AROMATICS, BY STATE

State	Number of plants	Quantity* (bbl/stream day)
California	3	5,990
Illinois	2	6,700
Kansas	1	1,400
Kentucky	1	4,000
Louisiana	3	19,100
Mississippi	1	6,000
New York	1	3,000
Oklahoma	1	2,000
Pennsylvania	3	9,700
Texas	18	122,525
Total	34	180,415

*Total quantity of benzene, toluene, and xylene produced.

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Table 3. ESTIMATED SIZE AND PRODUCTION CAPACITY OF BY-PRODUCT COKE PLANTS IN THE UNITED STATES ON DECEMBER 31, 1975

State	Number of plants[a]	Number of batteries	Number of ovens	Maximum annual theoretical production capacity (tons)	Coke production in 1974 (tons)
Alabama	7	28	1,401	6,961,000	5,122,000
California	1	7	315	1,547,000	(b)
Colorado	1	4	206	1,261,000	(b)
Illinois	4	9	424	2,523,000	1,912,000
Indiana	6(7)	31	2,108	11,925,000	9,073,000
Kentucky	1	2	146	1,050,000	(b)
Maryland	1	12	758	3,857,000	(b)
Michigan	3	10	561	3,774,000	3,259,000
Minnesota	2	5	200	784,000	(b)
Missouri	1	3	93	257,000	(b)
New York	3	10	648	4,053,000	(b)
Ohio	12	35	1,795	9,960,000	8,842,000
Pennsylvania	12(13)	51	3,391	18,836,000	16,318,000
Tennessee	1	2	44	216,000	(b)
Texas	2	3	140	839,000	(b)
Utah	1	4	252	1,300,000	(b)
West Virginia	3(4)	13	742	4,878,000	3,555,000
Wisconsin	1	2	100	245,000	(b)
Undistributed	-	-	-	-	12,656,000
Total	62(65)	231	13,324	74,266,000	60,737,000

[a] Three plants are collocated.

[b] Included in undistributed.

Source: Sheridan, E. T., "Supply and Demand for United States Coking Coals and Metallurgical Coke," U.S. Department of the Interior, Washington, DC (1976).

Table 4. PLANTS USING BENZENE AS AN INTERMEDIARY IN THE MANUFACTURE OF OTHER CHEMICAL COMPOUNDS

Company	City	State	Chemical(s)
Reichhold Chem., Inc.	Tuscaloosa	Alabama	phenol
Witco Chem.	Carson	California	detergent alkylate
Std. Oil Co. of CA	El Segundo		cumene
Speciality Organics, Inc.	Irwindale		dichlorobenzene
Std. Oil Co. of CA	Richmond		phenol, detergent alkylate
Ferho Corp.	Santa Fe Springs		phenol
Std. Chlorine Chem Co., Inc.	Delaware City	Delaware	mono- and dichlorobenzene
Chem. Products Corp.	Cartersville	Georgia	dichlorobenzene
Clark Oil & Refining	Blue Island	Illinois	cumene, phenol
Koppers Co., Inc.	Cicero		maleic anhydride
Reichhold Chem., Inc.	Morris		maleic anhydride
Monsanto	Sauget		nitrobenzene, mono- and dichlorobenzene
Skelly Oil Co.	El Dorado	Kansas	cumene, phenol
Ashland Oil, Inc.	Ashland	Kentucky	cumene
Foster Grant Co.	Baton Rouge	Louisiana	ethylbenzene, styrene
Cos-Mar, Inc.	Corville		ethylbenzene, styrene
Tenneco, inc.	Chalmette		ethylbenzene
Rubicon Chem., Inc.	Geismar		nitrobenzene, aniline
Georgia Pacific Corp.	Plaquemine		phenol
Gulf Oil Corp.	Welcome		ethylbenzene, styrene
Continental Oil Co.	Baltimore	Maryland	detergent alkylate
Solvent Chem. Co., Inc.	Malden	Massachusetts	mono- and dichlorobenzene
Dow Chemical	Midland	Michigan	ethylbenzene, styrene, cumene, phenol, mono- and dichlorobenzene

(continued)

Table 4 (continued)

Company	City	State	Chemical(s)
First Mississippi Corp.	Pascagoula	Mississippi	nitrobenzene, aniline
Monsanto	St. Louis	Missouri	maleic anhydride
Montrose Chem. Corp. of Cal.	Henderson	Nevada	monochlorobenzene
American Cyanamid	Bound Brook	New Jersey	nitrobenzene, aniline
Union Carbide	Bound Brook		phenol
Reichhold Chem., Inc.	Elizabeth		maleic anhydride
Tenneco, Inc.	Fords		maleic anhydride
E. I. Du Pont	Gibbstown		nitrobenzene, aniline
Std. Chlorine Chem. Co.	Kearny		dichlorobenzene
Texaco, Inc.	Westville		cumene
ICC Industries, Inc.	Niagara Falls	New York	mono- and dichlorobenzene
Occidental Petroleum	Niagara Falls		monochlorobenzene
Solvent Chem. Co.	Niagara Falls		mono- and dichlorobenzene
Allied Chem. Corp.	Syracuse		mono- and dichlorobenzene
United States Steel	Haverhill	Ohio	phenol
Arco/Polymers, Inc.	Beaver Valley	Pennsylvania	styrene
Koppers Co., Inc.	Bridgeville		maleic anhydride
United States Steel	Clairton		phenol
Allied Chemical Corp.	Frankford		phenol
United States Steel	Neville Island		maleic anhydride
Gulf Oil Corp.	Philadelphia		cumene, chlorohexane
Phillips Petroleum	Guayama	Puerto Rico	cyclohexane
Commonwealth Oil	Penuelas		ethylbenzene, cyclohexane
Union Carbide Corp.	Penuelas		cumene, phenol
Exxon Corp.	Baytown	Texas	cyclohexane
E. I. Du Pont	Beaumont		nitrobenzene, aniline
Union Oil Co. of CA	Beaumont		cyclohexane
American Petrofina	Big Spring		ethylbenzene, styrene, cyclohexane
Phillips Petroleum	Borger		cyclohexane

(continued)

Table 4 (continued)

Company	City	State	Chemical(s)
Monsanto	Chocolate Bayou	Texas (con.)	cumene, phenol, detergent alkylate
Coastal States Gas	Corpus Christi		cumene
Sun Oil Co.	Corpus Christi		ethylbenzene, styrene, cumene
Union Pacific Corp.	Corpus Christi		cyclohexane
Dow Chemical	Freeport		ethylbenzene, styrene
Arco/Polymers, Inc.	Houston		ethylbenzene, styrene
The Charter Co.	Houston		ethylbenzene
Joe Oil, Inc.	Houston		no data
The Merichem Co.	Houston		phenol
Petro-Tex Chem. Corp.	Houston		maleic anhydride
El Paso Natural Gas	Odessa		ethylbenzene, styrene
Dow Chemical	Oyster Creek		phenol
Phillips Petroleum Co.	Phillips		detergent alkylate
Arco/Polymers, Inc.	Port Arthur		ethylbenzene
Gulf Oil Corp.	Port Arthur		cumene
Texaco	Port Arthur		cumene
Union Carbide Corp.	Seadrift		ethylbenzene, styrene
Phillips Petroleum Co.	Sweeney		detergent alkylate
Marathon Oil Co.	Texas City		cumene
Monsanto	Texas City		ethylbenzene, styrene
Standard Oil (Indiana)	Texas City		ethylbenzene, styrene, cumene
Union Carbide Corp.	Charleston	West Virginia	detergent alkylate
Koppers Co., Inc.	Follansbee		monochlorobenzene
Allied Chem. Corp.	Moundsville		nitrobenzene, maleic anhydride
PPG Industries, Inc.	Natrium		mono- and dichlorobenzene
Mobay Chem. Corp.	New Martinsville		nitrobenzene, aniline
American Cyanamide	Willow Island		nitrobenzene, aniline
Stimson Lumber Co.	Anacortes	Washington	phenol
Kalama Chemical	Kalama		phenol

Table 5. ESTIMATION OF ATMOSPHERIC EMISSIONS DUE TO BY-PRODUCT MANUFACTURING FACILITIES IN 1976

By-product	Production capacity[a] (10^6 kg)	Amount of benzene unaccounted for[b] (10^6 kg)	Benzene emission using emissivity factor[c] (10^6 kg)
Ethylbenzene	3894	120	2.41
Styrene	3211	-	4.82
Cyclohexane	2076	0	7.58
Cumene	1720	-	0.43
Phenol	1252	275	1.25
Nitrobenzene	483	-	3.38
Detergent alkylate	393	98	0.86
Monochlorobenzene	313	-	1.10
Aniline	314	24	7.41
Maleic anhydride	189	142	18.28
Dichlorobenzene	120	22	1.03
Total		682	48.55

[a] Source: SRI, 1976 Directory of Chemical Producers, as cited in PEDCO, Environmental, "Atmospheric Benzene Emissions," prepared for U.S. Environmental Protection Agency, RTP (1977).

[b] Calculated using material balances in Benzene Environmental Sources of Contamination, Ambient Levels and Fate, Life Sciences Division, Syracuse University Research Corporation, 1974.

[c] Calculated using emission factors for benzene per kg of product.

The contribution of auto exhaust to ambient benzene levels has been estimated at 1 to 4 ppb in inner city areas and less than 1 ppb in suburban areas (5). These estimates are in general agreement with the ambient air levels, although downtown Houston levels have been measured at an average of 8 ppb for the 0600 to 0900 hr period (an average of 29 days). The pervasiveness of auto-exhaust-derived atmospheric benzene contributes more to higher total benzene emissions than any other source. Yet emissions from motor vehicles are widely distributed and contribute to relatively low ambient levels. Emissions from benzene production, transport, storage, and use are localized and the exposure of the population near these sites may be greater than that of the general population. In a study of the exposure of service station and bulk loading operators (12,13), ambient air concentrations were measured at 0.1 to 9.4 ppm. The highest urinary phenol concentrations (a benzene metabolite) were 18 mg/L for service station operators, 10 mg/L for bulk loading facilities workers, and 48 mg/L for workers loading gasoline containing added (10 to 33 percent) benzene. Another recent study of benzene exposure in self-service filling stations found levels of 43, 121, and 647 ppb in the breathing zone of three customers (14).

One major source of benzene not considered in the above discussion is tobacco smoke. Cigarette smoke has been reported (15) to contain 47 ppm, (6.1 μg/40 mL puff) which is higher than the NIOSH-recommended maximum allowable concentration of 10 ppm. These levels of benzene are important to this study since smokers and their families would be exposed to higher than ambient concentrations of benzene.

Benzene is ubiquitous in air samples and is nearly always found in water samples. Table 6 summarizes the ambient monitoring data through 1974 (16-27). Benzene was found (17) in finished water from the Mississippi River, but not in the effluents from 60 industries that discharge into the Mississippi, suggesting that the benzene source is nonindustrial (3). Benzene is one of the organic compounds identified in drinking water in the United States (28) at a minimum concentration of <5.0 μg/L. It has been identified in the drinking water in Miami, FL, Ottumwa, IA, Philadelphia, PA, Cincinnati, OH, Washington, DC, and the White House (28,29) but was not detected in the drinking water of Seattle, WA.

In addition to the air sampling data in Table 6, RTI has quantitated benzene in air samples from a variety of locations all over the United States (1). In over 500 analyses to date, benzene has been detected in all samples. Sampling locations have included the Los Angeles Basin, Houston, TX, Kanawha Valley, WV, El Dorado, AR, northern NJ, and Baltimore, MD. Table 7 presents some of the quantitative results found by RTI.

Battelle (30) recently measured benzene in air, water, and soil at several facilities employing benzene. They found ambient air benzene levels ranged from 0.4 to 34.8 ppb. Water levels ranged from <1 ppb to a high of 179 ppb, which was found in a plant effluent. Soil levels also ranged from less than detectable (<2 ppb) to a high of 191 ppb. Care must be exercised in comparing data for ambient air because seasonal variations may be an important factor in the emission rate and air-soil partitioning of the benzene.

Table 6. AMBIENT MONITORING DATA FOR BENZENE

Reference	Type of sample	Geographical location	Sampling[a] method used	Analysis[a] technique	Quantities detected
Gordon and Goodley (1971)	water and mud	Lower Tennessee River	CCE liquid-liquid	GC-MS	not reported
U.S. EPA (1972)	finished water	Carrollton Plant, New Orleans	CCE	preparative GC	not attempted
Prillows (1971)	finished water	U.S. PHS Hospital Carville, LA			"trace" ppb-ppm range
Novak et al. (1971)	"polluted" and "pure" drinking water	Prague, Czechoslovakia	inert gas stripping	GC, GC-MS	~0.1 ppb
Williams (1965)	ambient air	Vancouver, Canada	cold trap - GC column	rapid heating into GC	1-10 ppb
Sonyer *et al.* (1971)	ambient air	vicinity of solvent reclamation plant	grab sample	direct injection into GC; MS, IR	23 ppm
Helligan *et al.* (1975)	ambient air	Los Angeles basin	cold trap - firebrick	rapid heating into GC	0.005-0.022 ppm (V/V)
Altschuller and Bellar (1963)	ambient air	Downtown Los Angeles	grab sample	direct injection into GC	0.015-0.06 ppm (V/V)
Lonneman et al. (1968)	ambient air	Los Angeles basin	cold trap -	rapid heating	aver. 0.015 ppm highest 0.057 ppm (V/V)
Grob and Grob (1971)	ambient air	Zurich, Switzerland	charcoal trap - carbon disulfide extract	GC-MS GC-FI	0.054 ppm
Stephens (1973)	ambient air	Riverside, CA	cold trap - GC column	GC-FI	0.007-0.008 ppm
Pilar and Graydon (1973)	ambient air	Toronto, Canada	cold trap - GC column	GC-FI	aver. 0.013 ppm; highest 0.097 ppm

[a] CCE = carbon chloroform extract; GC = gas chromatography; FI = flame ionization; IR = infrared spectroscopy; MS = mass spectrometry.

Table 7. CONCENTRATIONS OF BENZENE FOUND IN AMBIENT AIR BY RTI

Site	No. samples	Concentration (ppb)	
		Mean	Range
Bound Brook, NJ	1	-	3.3
Paterson, NJ	1	-	0.8
Clifton, NJ	1	-	trace
Newark, NJ	1	-	111
Fords, NJ	1	-	1.1
Passaic, NJ	1	-	0.8
Hoboken, NJ	1	-	trace
Edison, NJ	29	-	60 to trace[a]
Staten Island, NY	1	-	0.8
Los Angeles, CA	1	-	6.8[b]
South Charleston, WV	3	34 ± 21	58 - 20
Belle, WV	6	28 ± 48	125 - 0.3
Dominguez, CA	1	-	12.7
Houston, TX	3	2.5 ± 2.4	5.4 - 1.2
Pasadena, TX	2	-	2.4 - 0.5
Deer Park, TX	7	4.0 ± 4.5	0.8 - 12.2
St. Louis, MO	-	-	72 - 0.2
Magnolia, AR	12	0.39 ± 0.38[c]	0.08 - 1.5
El Dorado, AR	34	0.06 ± 0.40[d]	0.002 - 0.16
Baton Rouge, LA	14	1.0 ± 1.1	0.02 - 3.4

[a] Fence line monitoring downwind of a chemical dump, levels as high as 480 ppb were found.

[b] Downwind of a petrochemical facility, 260 ppb benzene was found.

[c] Samples for 12 24-hour periods were collected on the roof of a three-story building.

[d] Samples for 32 24-hour periods were collected on a water tower ∼20 to 30 m above ground.

Source: E. D. Pellizzari, Quantification of Benzene in 150 Ambient Air Samples, Final Report, EPA P.O. No. DA-7-43205, August 1977.

ROUTES OF EXPOSURE

For the general population, exposure occurs primarily through respiration of the benzene generated by motor vehicle use. The presence of high concentrations of benzene in cigarette smoke, previously mentioned affects not only smokers, but people around them in congested areas. These two routes of exposure represent a background that is highly variable among individuals and with time according to their personal daily routine. In addition, there are indications (17,18,28,29) that benzene may be present in significant concentrations in the drinking water in certain areas. Some individuals may receive large doses of benzene while using it as a solvent, through the use of gasoline for nonmotor vehicle uses, through the use of benzene-containing commercial products, or via other unidentified sources.

Information on benzene levels in food is sparce. It apparently occurs naturally in fruit, fish, vegetables, nuts, dairy products, beverages, and eggs. Quantitative data exist only for cooked meat, rum, and eggs. A report by the National Cancer Institute (31) estimated that an individual could ingest as many as 250 µg/day from these foods. This compares to 320 µg/day respired from continuous exposure to 1 ppb of benzene in air. The relative absorption of benzene via these two routes of exposure is uncertain.

BASIS OF SITE SELECTION

The sites for measurement of benzene body-burden levels for populations in the vicinity of benzene manufacturing plants and/or benzene industrial user facilities were selected based on meteorological, geographical, topological, and demographic data for the area surrounding the facility. Exposure via water and food was considered to be reasonably constant within a locale. High, medium, and low exposure sites were then selected based on the proximity to an identifiable benzene source. Individuals were monitored with personal samplers for their ambient air exposure for 6 to 8 hours prior to collecting the biological sample. Because benzene is excreted very rapidly during the first 3 to 4 hours after exposure, this exposure period is the most relevant to the study (6,8).

The data in Table 8 were used to assess the locations most likely to define the upper limit of the human body-burden and three locations were recommended for study. The first location to be evaluated was Houston, TX. Although it does not rank highest for human exposure, the time frame of the study required a southern location for the winter/early spring sampling. Subsequent sampling in summer was less restricted. St. Louis, MO, was the second choice. Several factors were considered in site selection in addition to a potential benzene-exposed population. For example, each of these locations is a metropolitan area where general urban exposure may be evaluated and, in each location, a suburban-to-rural population exists within a reasonable distance to serve as a control.

Table 8. ESTIMATED EXPOSURE OF POPULATIONS TO BENZENE

Location	Company	Emission rate (10^6 kg/yr)	Population exposed to >10 ppb benzene
St. Louis, MO	Monsanto Shell	4.64	190,200
Elizabeth, NJ	Reichhold	1.35	34,100
Houston, TX	Petrotex Joe Oil Arco/Polymers	2.22 NA 0.09	20,900
Cicero, IL	Koppers	0.483	10,200
Philadelphia, PA	Gulf Oil Corp.	0.325	7,800
Morris, IL	Reichhold	2.61	5,200
Texas City, TX	Monsanto Marathon Oil Co. Standard Oil (Ind.)	1.78 0.02	5,100
Freeport, TX	Dow	1.53	2,500
Neville Island, PA	U.S. Steel	1.74	2,400
Bridgeville, PA	Koppers	1.45	2,300

Source: S. J. Mara and S. S. Lee, Human Exposures to Atmospheric Benzene, EPA Contract 68-01-4314, Final Report, October 1977.

NA = not avaiable.

SECTION 5

METHOD DEVELOPMENT AND PRETEST EVALUATION OF FILLING STATION ATTENDANTS (AND TANK TRUCK DRIVERS)

The feasibility of measuring benzene body-burden required testing with both known exposed individuals and nonexposed individuals. A local population of occupationally exposed individuals was available in the form of filling station attendants and tank truck drivers. Additional information about the ability to assess body-burden could be obtained by retest of the individuals after a period away from the occupational exposure. This approach was incorporated into the pilot study described below.

In addition to designing the test protocol for the participants, there were several technical problems in the sampling and analysis that had to be solved before the pilot test could be implemented. Benzene must be analyzed in blood at 1 μg/L or less on a sample size of 10 mL or less. Previously reported methods (8,32) were sensitive down to 10 μg/L. The second technical development required was a portable or semiportable breath sampling device or spirometer. The solutions to these technical problems are discussed as a preface to the pilot study results.

EXPERIMENTAL PROCEDURES

The sampling and analysis protocols developed for this study are given in Appendix A and special equipment developed for breath sampling is described in Appendix B. The background, development, and validation is discussed below.

Benzene in Blood

After an initial attempt to use the Volatile Organic Analysis (VOA) purge technique for the recovery of benzene from blood, a headspace analysis was used similar to that described by Sato et al. (8,32) in which an aliquot of blood sample was sealed in a hypodermic syringe and equilibrated at 37°C with subsequent analysis of the headspace over the blood. To increase the sensitivity of this approach, a larger blood sample, 1 mL instead of 0.1 mL, and a larger syringe, 10 mL vs. 1 or 2 mL, were used. In addition, instead of taking a small aliquot of the headspace, the entire headspace was purged through a cryogenic trap, which was part of a sample loop of a gas chromatograph and could subsequently be placed in line and warmed to volatilize the benzene and inject it as a small discrete sample onto the column. Preliminary verification indicated that the laboratory air, which was introduced into the headspace prior to equilibration, contributed less than 0.3 ng total mass to the sample. Using outdated blood from a local blood bank, both spiked and blank samples were prepared. The control samples contained 500 μg/L. Blank samples were used as they were obtained from the blood bank. Duplicate samples of the control and blanks were analyzed. The benzene found in the blank was 1.8 ± 0.6 μg/L and in the controls, 123 ± 8 μg/L. Although the reproducibility on the controls was very good, improvement in the 25 percent recovery was desired.

The blood analysis procedure was modified by reducing the time for equilibration (see Appendix A). To speed the attainment of thermal equilibrium, the 10-mL glass syringes were preequilibrated at 37°, 1 mL of the blood was introduced, and the syringes were sealed and reequilibrated for 20 min. After the 20-min equilibration, the entire headspace was purged into a cryogenic trap, the contents of which can be injected onto a GC. The sample was then injected and the trap heated. This procedure was evaluated using pooled blood from two nonsmoking laboratory workers. Benzene was added to portions of the pooled blood to give concentration of 1, 5, 10, and 20 μg/L. Each of these concentrations was analyzed in duplicate along with the blank pooled blood. The average percent relative deviation of the benzene spiked samples was 4 percent over this range and a least squares linear regression of the values gave a correlation coefficient of 0.991. The principal difficulty with the detection and quantitation of benzene in blood at low levels is the appearance of a benzene peak in "blank" blood. This blank has been assessed by analyzing blood samples taken from three nonsmoker laboratory workers (the two used from the calibration above plus subject F). These blood samples were analyzed in duplicate to yield a blank value of 1.1 ± 1.2 μg/L (standard deviation). Based on this variability in the blank, 3.4 μg/L would have to be present to detect benzene with a 95 percent confidence level. A further modification of the procedure was made using "zero" grade air for filling the headspace rather than laboratory air. The result of this modification was the reduction of blank blood values from 1.1 ± 1.2 to 0.49 ± 0.39 μg/L. By this method, 1.6 μg/L of benzene would have to be found for the results to be significant at the 95 percent confidence level.

Benzene in Breath

A breath collection apparatus (spirometer), diagrammed in Figure B-1, was constructed for the collection of breath samples. The spirometer was tested using two smokers for a positive test. The blank used in this evaluation was a volume of purified air comparable to that collected during the tests drawn through the apparatus. Sample collections were performed in the laboratory. Subject A was a 100-kg male who normally smoked between 1 and 1.5 packs of cigarettes per day. Subject A was a laboratory worker; however, all uses of benzene were restricted and no exceptions had been made for the particular place of work for this individual. Subject B was a 60-kg male who smoked 1.5 packs of cigarettes per day. He was a shop worker fabricating both metal and wood pieces. There was some possibility of exposure to benzene through solvents or adhesives that he may have handled during the course of his activities. These subjects were chosen primarily to provide a positive test for the apparatus; however, the information obtained from these tests served to establish the dynamic range of benzene levels which might be encountered in later studies. The results of these tests are given in Table 9. Based on these preliminary data the breath sampling protocol in Appendix B was developed.

PRETEST EVALUATION OF FILLING STATION ATTENDANTS AND TANK TRUCK DRIVERS

The pretest was designed to measure as many of the exposure and body-burden parameters as possible for the nine participants. Participants A and B were selected as controls for smokers and participants F and G were selected as control nonsmokers. The other participants were occupationally exposed for one sample collection period and presumably unexposed (nonworking) during the second sample collection.

After soliciting participation in the study, a schedule was set up with the subject. The schedule consisted of (1) initiation of personnel monitoring of benzene levels in air, (2) 6 to 8 hours after initiation of air monitoring, collection of a blood sample followed immediately by collection of a breath sample, and (3) collection of urine samples at this time for some participants. This sequence was performed first on a workday, then on a nonworkday. At least 18 hours lapsed between the last work exposure and the nonworkday blood collection.

Results and Discussion of the Pretest

The results of the pretest of benzene body-burden are given in Table 10. Inspection of the data indicates one line that is unique and uncharacteristic. Subject C on the work day test had unusually high blood and breath values. The exposure of this participant was probably atypical due to direct contact with gasoline containing benzene. The personnel monitor may not have fully registered this exposure because of possible skin absorption and high air concentration gradients possible with this type of exposure. The blood and breath levels are not those expected to be characteristic of environmentally exposed individuals. For these reasons, Subject C's data were excluded from the statistical evaluation. Excluding the Subject C workday data set, the correlation coefficients, slopes, and intercepts were calculated for the various parameters. Given sufficient data, the slopes would indicate the partition of benzene between the various phases such as blood and breath. The intercept indicates any residual benzene that is not related to the concentration in the phase being compared. For example, the intercepts for air vs. blood and air vs. breath are larger where smokers are included in the regression analyses indicating an exposure, smoking, that is not dependent on air benzene concentration. These parameters are given in Table 11. In every category, the correlation is better for nonsmokers than for smokers. The uncertain nature of the benzene exposure through smoking is the probable source of this variability. Air exposure and blood levels also correlate at the 95 percent confidence level in each category.

Breath vs. Blood--

The correlation of breath and blood levels is of particular concern, since it would permit estimation of body-burden from breath levels. Sato et al. (8) measured blood and breath levels kinetically following a 2-hr

Table 9. BENZENE IN BREATH--VALIDATION OF COLLECTION

Sample	Cigarettes (packs/day)	Sex	Weight (kg)	Benzene found in breath	
				μg/m³	ppb
A (laboratory worker)[a]	1.5	M	100	9.3[b]	3.1
B (shop worker)[c]	1.5	M	60	19[b]	6.5

[a] Laboratory air was found to contain 8.2 μg/m³ (2.7 ppb).

[b] Corrected for 1.7 μg/m³ in the air supply blank.

[c] No data on air levels.

Table 10. RESULTS OF PRETEST STUDY OF BENZENE BODY-BURDEN

						Benzene levels found						
						Air monitor		Breath			Blood	Urine
Sample	Occupation	Smoker or non-smoker	Sex	Weight (Kg)	Worked or off preceding test	($\mu g/m^3$)	(ppb)	($\mu g/m^3$)	ppb	(ng/min)	μg/L	μg/L
A	Laboratory worker	smoker	M	100	worked	a	a	9.3	3.1	87	-	
B	Shop worker	smoker	M	60	worked	a	a	19.0	6.5	110	-	
C	Filling station attendant	smoker	M	60-70	worked[b] off	153 -	48 -	432.0 6.8	136.0 2.1	2300 60	186.6 ± 1.4 0.42 ± 0.07	
D	Filling station attendant	smoker	M	80-90	worked off	260 13	82 4	17.0 11.0	5.4 3.5	98 57	1.88 <0.35	
E	Filling station attendant	non-smoker	M	90-100	worked off	-[c] 13	-[c] 4	7.2 1.3	2.3 0.4	40 8.4	0.28 ± 0.06 <0.34	
F	Laboratory worker	non-smoker	M	60	worked	a	a	1.1	0.4	7.3	0.1	
G	Laboratory worker	non-smoker	M	70-80	worked	a	a	3.7	1.2	10.4	d	0.72 ± 0.14[e]
H	Filling station attendant	smoker	M	60-70	worked off	190 1.4	60 0.4	27 15	8.4 4.7	200 130	1.14 0.40 ± 0.06	0.93 ± 0.14 0.41 ± 0
I	Gasoline tanker driver	non-smoker	M	60-70	worked off	54 85	17 27	58 28	18 8.4	513 246	1.30 ± 0.34 1.93 ± 0.12	2.4 ± 0.4 1.6 ± 0

[a] The individuals were not monitored; however, air monitoring in the vicinity of their work areas indicated 8.2 $\mu g/m^3$ of benzene in the air.

[b] Subject C had been repairing a fuel line on an automobile. It is probable that he was exposed to more benzene than indicated by the personnel monitor.

[c] Cartridge lost due to breakage.

[d] Interfering peak on the gas chromatogram.

[e] Sample taken on the same subject at a later date.

Table 11. LINEAR REGRESSION ANALYSIS OF THE BENZENE AIR EXPOSURE, BREATH AND BLOOD BENZENE LEVELS IN THE PRETEST

	Smokers				Nonsmokers				All subjects			
	Slope	Intcp	r	n	Slope	Intcp	r	n	Slope	Intcp	r	n
Breath[a] vs. Blood[b]	0.051	0.011	0.55	5	0.025	0.28	0.75	5	0.026	0.32	0.64	10
Air[a,c] vs. Blood[b]	0.0058	0.22	0.97	4	0.023	-0.018	0.997	4	0.0060	0.42	0.75	8
Air[a,c] vs. Breath[a]	0.032	14	0.57	6	0.52	1.0	0.72	5	0.056	14	0.30	11
Blood vs. Urine	-	-	-	-	-	-	-	-	0.90	0.26	0.66	4

[a] Benzene concentration in μg/m^3 was used.

[b] "Less than" values treated as one-half the given value.

[c] Some air data were estimated by the value found for laboratory air (8.2 μg/m^3).

Key: intcp = intercept of linear regression
r = correlation coefficient
n = number of measurements

exposure to 25 ppm of benzene. From these data, the ratio of blood concentration (μg/L) to breath level (μg/m^3) is 0.016 (range, 0.012 to 0.018). This ratio represents the average of the ratios for 0, 60, 120, and 240 min after the termination of the exposure. A comparison of Sato's ratio and the slopes obtained from the linear regression of breath and blood levels shows similar values in the case of nonsmokers and all subjects. The similarity of the blood-breath ratios indicates that the blood/breath relationship at the ppb level and ppm level of benzene exposure is similar. The correlation of the pretest blood/breath data ($r = 0.64$) is significant at the 95 percent confidence level for all subjects ($n = 10$).

Further justification for the use of breath as a measurement of body-burden may be made based on the prediction that a large number of blood values will be less than the detection limit. For blood, the significant value has been estimated by obtaining blood from "unexposed" nonsmokers and determining the benzene. The average value of a total of six measurements of blood from three individuals was 0.49 ± 0.39. At the 95 percent confidence level, 1.6 μg/L of benzene would need to be found to be significantly different from 0.49 μg/L. It is improbable that every individual in even the highest environmentally exposed population would have blood benzene levels above 1.6 μg/L. On the other hand, breath samples have shown benzene levels discernible above the blank at all exposure levels. The dynamic range is thirtyfold (highest over lowest values) for breath relative to about fourfold over a background of 0.49 μg/L for blood. This dynamic range is especially important because three exposure groups were to be examined. Blood levels would not be able to differentiate between the low and medium exposure groups and only if the high exposure groups have individuals exposed to significantly greater than 30 μg/m^3 would detectable levels of blood benzene be found. It should be pointed out that the detection limit reported here for blood is more than an order of magnitude lower than that previously reported in the literature. Reproducibility of the breath analyses is good as indicated by the analysis of the replicate breath cartridge from Subject A where the difference between the two determinations was 5.8 percent.

Urine--

Urine analysis was included for the last two subjects. The values are similar to those of blood as would be anticipated if no active transport occurred in the kidney. Current data are insufficient to assess the validity of this relationship.

Air vs. Blood and Breath--

Although air exposure and breath levels do not correlate well for the nine individual samples, measurements of air exposure are still necessary for proper assessment of subject exposure in the study because of the daily fluctuations of benzene concentration in air and the short biological half-life of benzene. The cartridge used in the pretest was too bulky to locate in the subject's breathing zone so it was attached at the subject's waist). For an environmentally exposed subject, this would not be a serious problem since local concentration gradients would be small. For the pretest subjects, however, highly localized exposures probably occurred (e.g., height of gas pump nozzle), which may contribute to the lack of good correlation with exposure.

If the test subjects are divided into two groups, those exposed to <30 μg/m^3 and those exposed to >30 μg/m^3, and one computes the coefficients of variation (Table 12), an idea of the type of information one might obtain for a high vs. low exposure group is obtained. Table 12 indicates that the relative variability in the breath levels (80.2 percent and 54.4 percent) is much greater than for the blood levels (43.3 percent and 25.7 percent). Since the sample individuals were selected to represent a wide range of exposure levels, this would indicate that breath measurements may be more sensitive than blood measurements to changes in exposure.

The complicated kinetics of absorption and excretion of benzene make detailed analysis of body-burden difficult. It is clear from the pretest that if exposure is sufficiently high, breath and blood levels are elevated and the two correlate at the 95 percent confidence level. Because of its greater range, breath is more likely to differentiate between the high, medium, and low exposure populations. Although blood and breath correlate at the 95 percent confidence level with 10 paired measurements, a larger number of measurements would be desirable. Since only the high exposure population of the performance sites was expected to contain individuals with measurable blood levels of benzene, the incorporation of this matrix in the study was made in the interest of improving the sample size for the blood/breath correlation. The added effort to include the blood samples was small compared to the information content. The inclusion of blood samples from the other two groups was unlikely to produce any significant additional data because of the large number of nondetectable levels anticipated.

Effects of Smoking--

Smokers had consistently higher benzene levels than nonsmokers. Further evidence of the effect of smoking on benzene levels in breath is found in the results of the pilot study presented in "Formulation of a Preliminary Assessment of Halogenated Organic Compounds in Man and Environmental Media" (32). In this pilot study, breath samples from residents of the Love Canal area of Niagara Falls, NY, were analyzed for halogenated hydrocarbons and other toxic organics. Quantitation of the benzene levels was also performed. The results are given in Table 13. Smokers in this group had breath concentrations ranging from 1.8 to 7.0 μg/m^3 while nonsmokers had breath benzene levels ranging from 0.69 to 0.90 μg/m^3. Pooling all the data from the pretest and the Love Canal study for those individuals where occupational exposure was not contributory to benzene body-burden, one finds a mean breath benzene level of 1.33 μg/m^3 with a standard deviation of 1.06 ($n = 7$) for nonsmokers while the mean was 8.42 μg/m^3 for smokers (standard deviation was 5.38 with $n = 10$). The difference is significant at greater than 99.5 percent confidence level.

Clearly, smoking is a major contributory factor to benzene body-burden. Since the objectives of this study were to evaluate environmentally related (nonsmoking) benzene body-burden, smokers were excluded from the main study. It was felt that inclusion of smokers would confound the data and require a much larger sample size.

Table 12. SAMPLE STATISTICS FOR BLOOD AND BREATH FOR TWO INTERVALS OF AIR EXPOSURE

Air exposure	Breath	Blood (μg/L)
<30 μg/m^3		
mean	8.6	.30
std. dev.	6.9	.13
range	1.1 to 19	.1 to .4
C.V.	80.2	43.3
>30 μg/m^3		
mean	32.5	1.56
std. dev.	17.7	.40
range	17 to 52	1.14 to 1.93
C.V.	54.4	25.7

C.V. = (std. dev./mean) x 100

Table 13. ESTIMATED LEVELS OF BENZENE IN HUMAN BREATH FROM "OLD LOVE CANAL" IN NIAGARA FALLS, NY

Participant no.	Smoker or nonsmoker	Benzene (μg/m^3)
10009	smoker	1.8 ± 0.12
10017	smoker	2.6 ± 1.6
10025	nonsmoker	0.90
10033	smoker	6.8 ± 0.8
10066	nonsmoker	0.69
10041	smoker	7.0 ± 1.6
10058	nonsmoker	0.90
10074	smoker	4.9
10090	nonsmoker	0.74 ± 0.13

Source: E. D. Pellizzari, letter to Joseph Breen, Office of Toxic Substances, U.S. Environmental Protection Agency, concerning the Pilot Study at Love Canal under EPA Contract No. 68-01-4731, September 1978.

SECTION 6

SAMPLE DESIGN AND SELECTION

The pretest with the filling station attendants and others at the RTI laboratory served to test the chemical sampling and analysis methods. The pilot studies conducted in Harris County, TX (Houston), and St. Louis, MO-Woodriver/Roxana/Hartford, IL (St. Louis), served as tests of the sample design and field operations. The strategy and rationale for the sample design are discussed below with improvements that were made between the two sites.

HOUSTON, TX, AREA SITE

Overview

The sample design can be described as a two stage-design with stratification imposed at the first-stage. First-stage sampling units were clusters of housing units, called segments, within which a sample of eligible persons was selected at a second stage of sampling.

Two dimensions of stratification were imposed on the first-stage frame. The dimensions employed controlled the distribution of the sample with respect to geography and degree of exposure to benzene. A total of 15 separate stratum cells were defined over each dimension. A total of 30 first-stage units were selected with equal probability and without replacement. The first-stage sample was equally allocated among the three exposure areas making up the first dimension of stratification.

For each first-stage unit, a second-stage sample of eligible person was selected so that equal weights would apply within the three exposure areas. The sample was selected with equal probability and without replacement. A total of 151 eligible persons were selected at the second stage.

Target Population

The target population was the residents of Harris County, TX. Three geographical areas were designated as high, medium, and low exposure areas.

The population was restricted to those individuals residing in the target areas during the data collection period. They also had to be in their places of residence at night.

The population was restricted to specific types of individuals. The following criteria were used in defining the target population:

1. 25 to 50 years old;

2. Nonsmokers;

3. Nonoccupationally exposed; specifically, a person was not considered eligible if employed as a painter or in a service station, garage, furniture repair shop, or chemical plant;

4. Not engaged in any hobbies involving exposure to high levels of benzene; specifically, painting, building models, gardening, or refinishing furniture;

5. Healthy individuals, i.e., taking no prescription medicine.

First-Stage Area Sample

Construction of the First-Stage Frame--

The sample was a probability sample of area segments. Being an area sample, the sampling frame had to be constructed so that all land area defined in Harris County, TX, was included in the frame and no area was included more than once. For this purpose, 1970 Census Enumeration Districts (EDs) and Block Groups (BGs) were used. These are units for which information about the number of housing units was available for use in defining sampling units.

Stratification of the First-Stage Frame--

The first dimension of stratification was designation of three geographical areas as high, medium, and low exposure areas. The high exposure stratum consisted of the blocks in the city of Houston, TX, shown crosshatched in Figure 1. The tracts and block groups are listed in Table 14.

The medium exposure stratum was all of the area in the city of Houston, TX, that was not part of the high exposure stratum. The areas are shown in Figure 1.

The low exposure stratum was all the area in Harris County, TX, not in the city of Houston. The areas are shown in Figure 1.

To compensate for meteorological variability, the areas radiate in all directions. This was accomplished by using a second dimension of stratification. Each of the three exposure areas (major strata), were divided into five strata (minor strata) as follows:

1. The total number of housing units in each of the three major stratum was determined from the 1970 census data.

2. These numbers were divided by 5. This was the approximate size of each of the five minor strata.

Table 14. HIGH EXPOSURE AREA, HOUSTON, TEXAS -- MINOR STRATA

1		2		3		4		5	
Tract[a]	BG[a]	Tract	BG	Tract	BG	Tract	BG	Tract	BG
320	101	320	221	322	507	322	207	321	107
	103		222		106		202		108
	113		223		801		208		109
	105		225		721		213		110
	109		224		720		212		224
	116		226		803		211		223
	117		301		806		210		221
	118	323	102		807		209		220
	120		504		810		201		111
	121		505		811		120		112
	122		506		814		118		113
	123				815		116		114
	124				813		115		115
	125				812		119		116
	126				809		114		219
	127				808		113		311
	128				805		112		312
	129				804		111		320
	130				719		110		321
	131				217		109		322
	132				216		107		323
	133				205		106		324
	201				206		105		227
	219				215		817		228
	220				214		820		229
							819		301
						321	102		302
							103		303
							226		304
							225		305
							104		332
							105		331
							106		330
									329
									406

[a] 1970 Census.

BG = Block Groups.

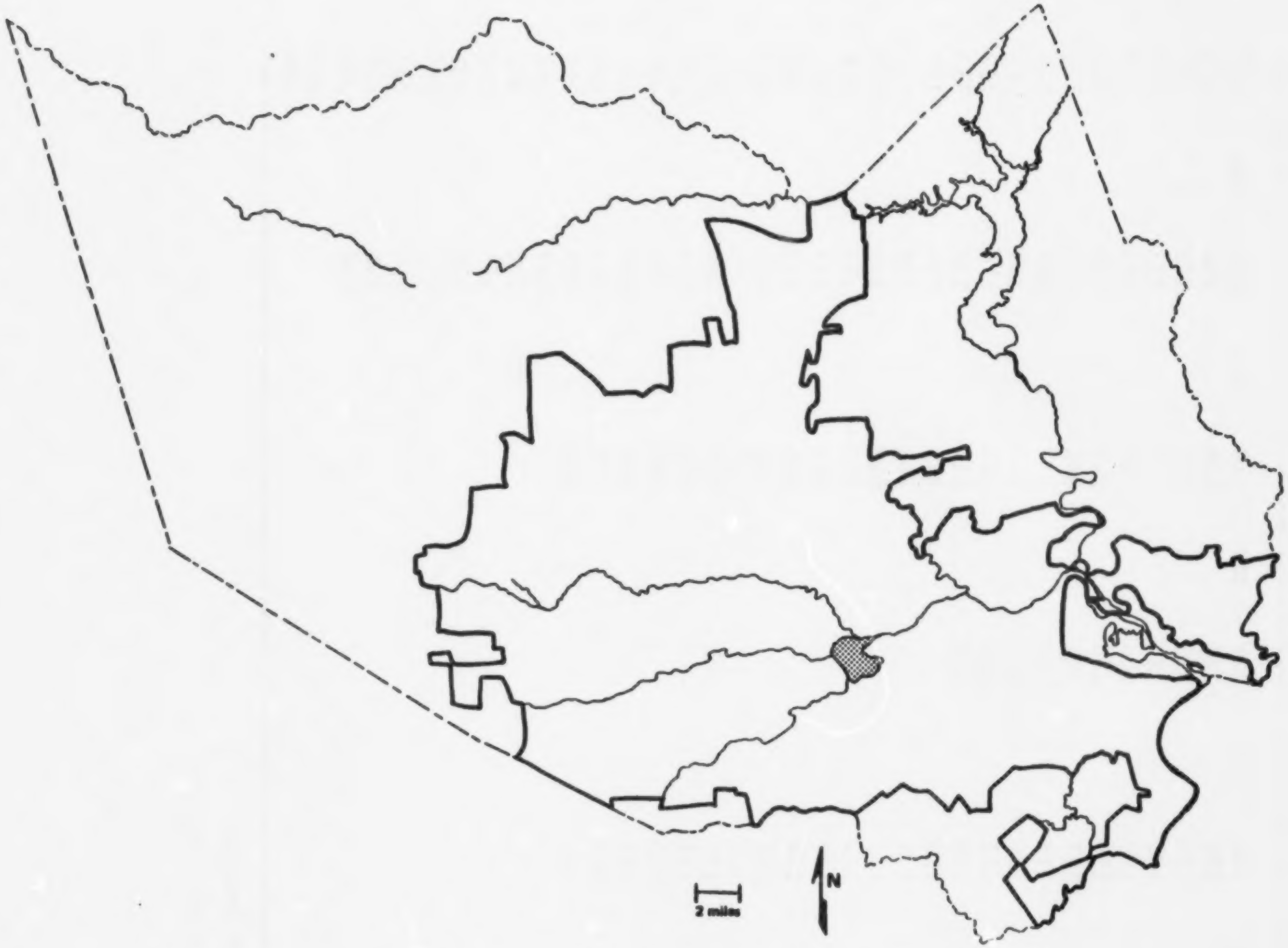


Figure 1. Map of Harris County, TX, showing the various exposure areas; shaded = high exposure, area enclosed in bold line = medium exposure, and remainder = low exposure.

3. The file for each of the major strata was ordered by Tract, Block Group, and/or Enumeration District.

4. Starting with the lowest numbered Tract, Enumeration District and/or Block Group, the number of housing units was accumulated until this number was less than or equal to this minor stratum size. The next Block Group or Enumeration District was added or omitted depending on whether the admission or omission made the stratum size closer to the ideal stratum size. These tracts with their BG/EDs were called minor stratum 1. This procedure was continued until all five minor strata were formed.

This stratification scheme defined 15 unique minor strata.

Selection of the First-Stage Sample--

Sampling units were assigned to each stratum so that the sampling unit contained approximately 25 housing units. This was accomplished by dividing the stratum's total number of housing units by 25 then rounding to the nearest integer. The total number of sampling units assigned to each stratum is shown in Table 15. Each stratum's total sampling unit was then distributed across the stratum's EDs and BGs based on the ED's or BG's total number of housing units. To accomplish this step, a list of all EDs and BGs in the stratum and their associated population was prepared from 1970 census data. The housing units were then accumulated across this list so that each ED and BG had an accumulated number of housing units representing the sum of its total number of housing units and all housing units in EDs and BGs previous to it on the list. The accumulated number of housing units was divided by the expected number of housing units in the stratum then rounded to the nearest integer to determine the accumulated number of sampling units. The number of sampling units assigned to each ED and BG was then determined by subtracting the EDs or BGs accumulated number of sampling units from the immediately preceding EDs or BGs accumulative sampling units. Any ED or BG that did not have enough housing units to be assigned one sampling unit was combined with other EDs or BGs in close geographic proximity until at least one sampling unit could be assigned to the combination. The two sampling units allocated to the stratum were then selected from all sampling units in the stratum with equal probabilities and without replacement. This was done by selecting two random numbers in the range from one to the total number of sampling units in the stratum.

Identification of Sampling Units Within EDs and BGs--

When a selected sampling unit fell within a BG or combination of BGs, its location was determined and housing unit data for the individual blocks forming the BG were compiled. The total number of sampling units assigned to the BG was then distributed across the individual blocks based on their total housing units. Thus, if t were the total number of sampling units assigned to a selected BG and t_i was the number of sampling units assigned to block i within the selected BG, then $0 \leq t_i \leq t$ and $\Sigma t_i = t$. Any block assigned $t_i = 0$ sampling units was combined with another block or block so that the combination had a positive number of sampling units. Any units, single block, or combination of blocks having a positive number of sampling units was called a segment with u_i sampling units. A sampling unit, k,

Table 15. STRATUM HOUSING UNIT DATA AND SAMPLE ALLOCATION

High exposure				Medium exposure				Low exposure			
Stratum	Number of HUs	Number of SUs	Expected size of SU	Stratum	Number of HUs	Number of SUs	Expected size of SU	Stratum	Number of HUs	Number of SUs	Expected Size of SU
1	670	27	24.82	1	113867	4555	25.00	1	4661	186	25.06
2	721	29	24.86	2	114003	4560	25.00	2	5042	202	24.96
3	674	27	24.96	3	113905	4556	25.00	3	4934	197	25.05
4	718	29	24.76	4	113880	4555	25.00	4	4834	193	25.05
5	687	29	23.69	5	113753	4550	25.00	5	4717	189	24.96
Total	3,470	141	24.61	Total	569,408	22,776	25.00	Total	24,188	967	25.02

HU = Housing unit.
SU = Sampling unit.

within a segment, i, was defined as the cluster of housing units beginning with the kth housing unit in a list of housing units to be compiled by field personnel, $1 \leq k \leq u_i$, and then taking every u_ith housing unit thereafter. Thus, the random number identified the selected sampling unit located in a particular segment and determined the particular sampling unit within the segment by identifying it by a start number, k, and a rate $1/u_i$. The selected samples are shown in Table 16.

The selected first-stage sampling units were counted and listed (see Section 7). The actual housing unit counts are shown in Table 17. The expected number of housing units and the actual number of housing units in both the high exposure and medium exposure areas were very close; however, in the low exposure area the actual number was much greater than the expected number of housing units. There were too many housing units to screen. To reduce the screening costs, these segments were subsampled by taking an equal probability without replacement samples. The sample sizes are shown in Table 16.

Selection Of the Second-Stage Sample

Construction of the Second-Stage Frame--

The sampling frame at this stage was simply the list of all household members who met the criteria specified above and who agreed to participate in the Survey.

Selection of the Second-Stage Sample--

From the list of eligible persons in each segment, an equal probability without replacement sample was selected. The sample sizes are shown in Table 18.

Calculation of Sampling Weights

For convenience, the notations used in this selection are summarized below:

h = 1, 2, . ., 5 indexes the minor stratum cells.

i = indexes the first stage units; values of i are nested within h.

N(h) = the number of first-stage units, cluster of housing units called segments, in the h-th stratum.

n(h) = the number of first-stage units, segments, selected from the h-th stratum (two).

M(hi) = the number of households in the (hi)-th first-stage unit.

m(hi) = the number of households selected from the (hi)-th first-stage unit.

N(hi) = the number of eligible persons who agreed to participate at the time of screening in the (hi)-th first-stage unit.

Table 16. SELECTED SAMPLES -- HOUSTON, TX

Stratum	High exposure				Medium exposure				Low exposure			
	Number of HUs (1)	Segment		Sampling units	Number of HUs (1)	Segment		Sampling units	Number of HUs (1)	Segment		Sampling units
		Tract	Blocks			Tract	BG/ED			Tract	BG/ED	
1	35	320	124	1/1-1	24	233	203	1/1-1	126	250	4	1/4-1
	35	320	127,128	1/1-1	25	208	217,218	1/1-1	91	228	202,909 910	1/3-2
2	116	320	222	1/5-4	71	327	207	1/3-1	106 (2)	258	81A	1/4-3
	116	320	222	1/5-4	37	302	205	1/1-1	37	251	310,311	1/1-1
3	13	322	814	1/1-1	34	409	309,310	1/1-1	121	452	431	1/4-4
	31	322	813	1/1-1	574	403	502	1/23-12	32	533	106	1/2-2
4	21	322	119	1/1-1	17	433	106	1/1-1	104 (2)	538	144	1/4-2
	119	322	106,107	1/4-3	78	431	501	1/3-1	102 (2)	545	174	1/4-3
5	22	321	110	1/1-1	21	506	212	1/1-1	129 (2)	551	175	1/5-5
	17	321	111	1/1-1	37	519	217	1/2-1	132 (2)	556	142	1/6-2

HU = Housing unit.
SU = Sampling unit.

Table 17. HOUSING COUNTS PER SEGMENT FOR HOUSTON, TX

	High exposure			Medium exposure			Low exposure			
		No. housing units			No. housing units			No. housing units		
Stratum	Segment	70 Census	Actual	Segment	70 Census	Actual	Segment	70 Census	Actual	Sample Size
1	11	35	34	28	24	27	38	32	73	20
	12	35	34	29	25	22	33	30	561	52
2	13	23	24	27	24	24	39	27	71	20
	19	23	24	26	37	35	37	37	56	20
3	14	13	12	25	34	34	36	30	168	30
	15	31	31	24	25	25	34	16	18	18
4	16	21	15	20	17	21	31	26	197	39
	17	30	29	21	26	26	35	26	190	22
5	18	22	16	22	21	19	30	26	174	20
	10	17	21	23	19	14	32	22	253	23

Table 18. SAMPLE SIZES OF ELIGIBLE PERSONS FOR HOUSTON, TX

	High exposure				Medium exposure				Low exposure			
		Eligibles				Eligibles				Eligibles		
Stratum	Segment	Total	Selected	Responded	Segment	Total	Selected	Responded	Segment	Total	Selected	Responded
1	11	10	8	5	28	7	7	0	38	0	0	0
	12	7	7	4	29	10	10	1	33	22	10	4
2	13	3	3	0	27	8	8	3	39	8	2	0
	19	2	2	1	26	9	9	2	37	11	2	1
3	14	5	5	0	25	7	7	2	36	9	3	2
	15	4	4	2	24	4	4	2	34	4	2	1
4	16	2	2	0	20	5	5	1	31	9	2	0
	17	7	7	4	21	11	11	3	35	10	3	1
5	18	7	7	0	22	9	4	3	30	7	3	2
	10	2	2	0	23	6	6	1	32	10	6	5
	Total	49	47	16	Total	76	71	18	Total	90	33	16

n(hi) = the number of eligible persons who participated from the (hi)-th segment.

As discussed previously, the actual number of housing units found in the selected first-stage units in the low exposure area was much greater than the expected number; therefore, the first-stage units were subsampled before they were screened. Thus, the calculation of the weights for the low exposure area requires a different formulation than the calculation of the weights for both the high exposure and low exposure areas.

Since the calculation of the weights for both the high exposure and medium exposure areas is simpler than for the low exposure area, it will be presented first followed by the weight calculation for the low exposure area.

Calculation of the Sampling Weights for Both the High and Medium Exposure Areas--

The selection probability for an eligible person is given by

$$\pi(hij) = \frac{2}{N(h)} \frac{n(hi)}{N(hi)} \tag{1}$$

for all

$j = 1, 2, \ldots, n(hi)$

eligible persons who participated in the (hi)-th segment.

The sample weights are the reciprocal of the selection probabilities given by

$$w(hij) = 1/\pi(hij) \tag{2}$$

for all

$j = 1, 2, \ldots, n(hi)$

eligible persons in the (hi)-th segment.

Calculation of the Sampling Weights for the Low Exposure Area--

The selection probability for an eligible person is given by

$$\pi(hij) = \frac{2}{n(h)} \frac{m(hi)}{M(hi)} \frac{n(hi)}{N(hi)} \tag{3}$$

for all

$j = 1, 2, \ldots, n(hi)$

eligible persons who participated in the (hi)-th segment.

The sample weights are the reciprocal of the selection probabilities given by

$$w(hij) = 1/\pi(hij) \tag{4}$$

for all

$$j = 1,2, \ldots, n(hi)$$

eligible persons in the (hi)-th segment. The sample weights are shown in Table 19.

Nonresponse Adjustment

A nonresponse compensation was made by using n(hi), the number of eligible persons who participated in the sample, rather than the number of eligible persons selected for the sample in the weight calculations. This is the same as using the average value of the response variable of the responding eligible persons for the nonrespondents in the same segment.

ST. LOUIS, MO, AREA SITE

Overview

The sample design can be described as a two-stage design with stratification imposed at the first-stage. First-stage sampling units were clusters of housing units, called segments, within which a sample of eligible persons was selected at a second stage of sampling.

Two dimensions of stratification were imposed on the first-stage frame. The dimensions employed controlled the distribution of the sample with respect to geography and degree of exposure to benzene. A total of nine separate stratum cells were defined over each dimension. A total of 18 first-stage units were selected with equal probability and without replacement. The first-stage sample was equally allocated among the three exposure areas making up the first dimension of stratification.

For each first-stage unit, a second-stage sample of eligible persons was selected so that equal weights would apply within the three exposure areas. The sample was selected with equal probability and without replacement. A total sample size of 75 eligible persons was designated to be selected at the second stage. Sample persons were defined as individuals between the ages of 25 and 50 years old.

Target Population

The target population consisted of the human population that resides in St. Louis City, St. Louis County, MO, and parts of Wood River, Roxana, South Roxana, and Hartford, IL. Three geographical areas were designated as high, medium, and low exposure areas.

Table 19. SAMPLING WEIGHTS FOR HOUSTON, TX

City	Exposure	Stratum	Segment	N(h)	n(h)	N(hi)	n(hi)	Weight
High exposure								
1	1	1	11	27	2	10	5	27.000
1	1	1	12	27	2	7	4	23.625
1	1	2	13	29	2	3	0	--
1	1	2	19	29	2	2	1	29.000
1	1	3	14	27	2	5	0	--
1	1	3	15	27	2	4	2	27.000
1	1	4	16	29	2	2	0	--
1	1	4	17	29	2	7	4	25.375
1	1	5	18	29	2	7	0	--
1	1	5	10	29	2	2	0	--
Medium exposure								
1	2	1	28	4,555	2	7	0	--
1	2	1	29	4,555	2	10	1	22,775.000
1	2	2	27	4,560	2	8	3	6,080.000
1	2	2	26	4,560	2	9	3	10,260.000
1	2	3	25	4,556	2	7	2	7,973.000
1	2	3	24	4,556	2	4	2	4,556.000
1	2	4	20	4,555	2	5	1	11,387.500
1	2	4	21	4,555	2	11	3	8,350.833
1	2	5	22	4,550	2	9	3	6,825.000
1	2	5	23	4,550	2	6	1	13,650.000

(continued)

Table 19 (continued)

Low exposure

City	Exposure	Stratum	Segment	N(h)	n(h)	M(hi)	m(hi)	N(hi)	n(hi)	Weight
1	3	1	38	186	2	73	20	0	0	--
1	3	1	33	186	2	561	52	22	4	5,518.298
1	3	2	39	202	2	71	20	8	0	--
1	3	2	37	202	2	56	20	11	1	3,110.800
1	3	3	36	197	2	168	30	9	2	2,482.200
1	3	3	34	197	2	18	18	4	1	394.000
1	3	4	31	193	2	197	39	9	0	--
1	3	4	35	193	2	190	22	10	1	8,334.091
1	3	5	30	189	2	174	20	7	2	2,877.525
1	3	5	32	189	2	253	23	10	5	2,079.000

The population was restricted to those individuals residing in the target areas during the data collection period. They also had to be in their places of residence at least 6 hours prior to the time the measurement was to be taken. The population was restricted to specific types of individuals. The following criteria were used in defining the target population:

1. 25 to 50 years old;

2. Nonsmokers;

3. Nonoccupationally exposed; specifically, a person was not considered eligible if employed as a painter or in a service station, garage, furniture rapair shop, or chemical plant;

4. Did not engage in any hobbies involving exposure to high levels of benzene; specifically, painting, building models or refinishing furniture;

5. Healthy individuals, i.e., taking no prescription medicine.

First-Stage Area Sample

Construction of the First-Stage Frame--

The sample is a probability sample of area segments. Being an area sample, the sampling frame was constructed so that all land area defined below was included in the frame and no area was included more than once. For this purpose, 1970 Census Enumeration Districts (EDs) and Block groups (BGs) were used. These are units for which information about the number of housing units was available for use in defining sampling units.

Stratification of the First-Stage Frame--

The first dimension of stratificaton was the designation of three geographical areas as high, medium, and low exposure areas. The high exposure stratum consisted of the following blocks in Wood River, Roxana, South Roxána, and Hartford, IL:

Stratum	Part	Boundary Streets
1	1	Satier Place, Clark, Thomas Street, Chaffer Ave., 8th Street, State Highway 111, Old Edwardsville Road, 6th Street, Esther Avenue
2	1	State Highway 143, Town Limits, Kindall Drive, Crestview Road, Arbitrary Line
	2	Arbitrary Line, Alton-Edwardsville Road, Town Limits

Stratum	Part	Boundary Streets
	3	Hedge Road, High Street, Washington Street, Park Street, Roxanna Street, Park Street, ID Boundary, State Highway 111, Roxana City Limits, Alton-Edwardsville Road, Madison Street
	4	Rand Avenue, Olive Road, 7th Street, IT Railway
3	1	Main Street, Evans Avenue, Wolcott Street, Arbitrary line
	2	Dulany Avenue, Ferguson Avenue, Madison Avenue, 8th Street, Esther Avenue, Old Edwardsville Road, 6th Street, Madison Avenue, Wood River Avenue, E. Lorena Avenue
	3	13th Street, Chaffer Street, Thomas Street, Dofier Avenue, 12th Street, Esther Avenue
	4	Trailer Park on Alton-Edwardsville Road

These areas are shown crosshatched in Figure 2.

The medium exposure stratum is all the area in St. Louis, MO, and St. Louis County roughly east of Interstate I-244 and I-270. The census tracts are shown in Figure 3.

The low exposure stratum is all the area in St. Louis County, MO, roughly west of Interstate I-244 and I-270. The census tracts are shown in Figure 3.

To compensate for meteorological variability, the areas radiate in all directions. This was accomplished by using a second dimension of stratification. Each of the two exposure areas (major strata), medium and low, were subdivided into three strata (minor strata) as follows:

1. The total number of housing units in each of the two major strata was determined from the 1970 census data.
2. These numbers were divided by 3. This was the approximate size of each of the three minor strata.
3. The file for each of the major strata was ordered by Tract, Block Group, and/or Enumeration District.
4. Using a tract map along with the file having data, the three minor strata were formed as shown in Figure 3.

The high exposure area was subdivided into three strata (minor strata) as follows:

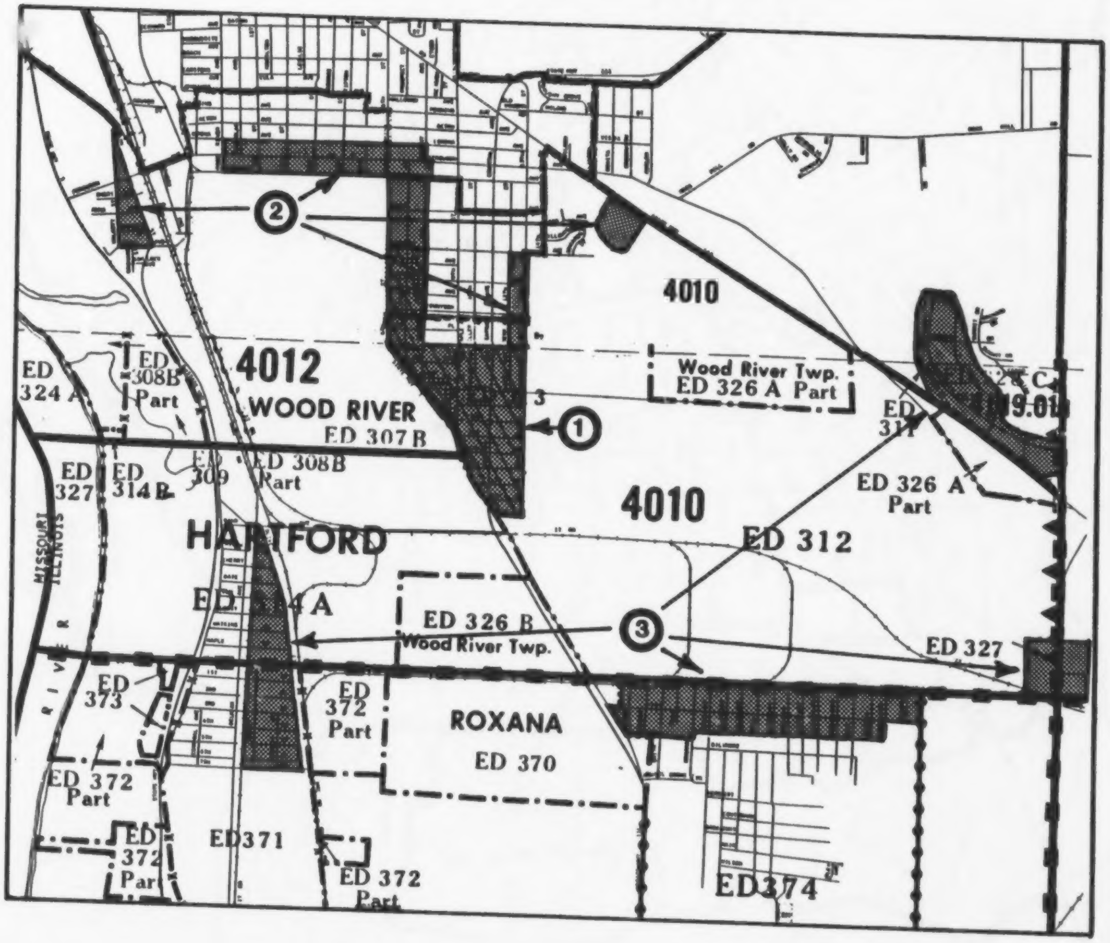
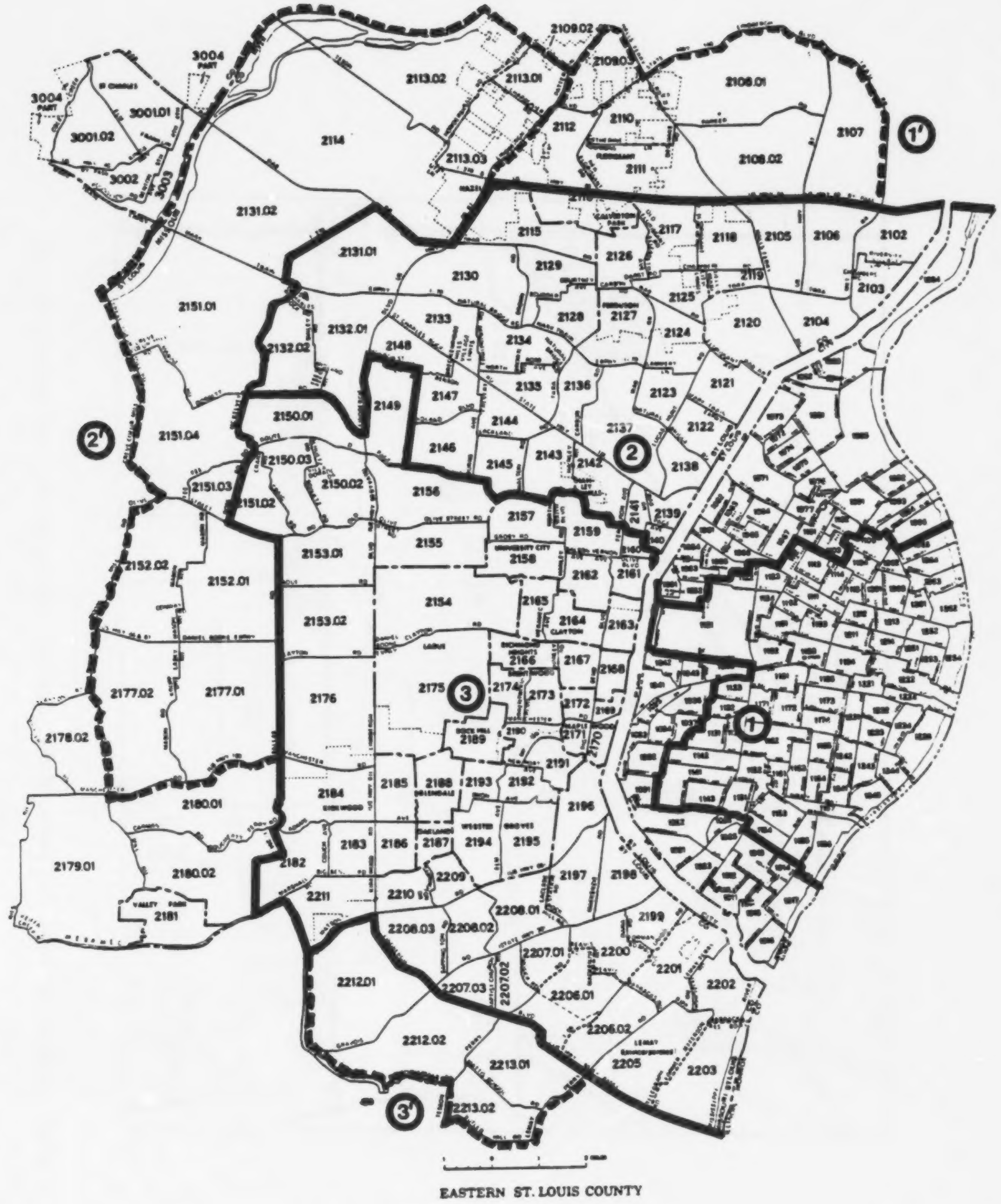

①
②
③
4010
4010
4012
WOOD RIVER
ED 307 B
Wood River Twp.
ED 326 A Part
ED 324 A
ED 308B Part
ED 327
ED 314 B
ED 309
ED 308B Part
HARTFORD
ED 314 A
ED 311
ED 326 A Part
ED 312
ED 326 B
Wood River Twp.
ED 327
ED 373
ED 372 Part
ROXANA
ED 370
ED 372 Part
ED 372 Part
ED371
ED 372 Part
ED374
MISSOURI
ILLINOIS
RIVER

Figure 2. High exposure strata for Wood River, Roxana, South Roxana and Hartford, IL.


1'
2'
3'
1
2
3
3004 PART
3001.01
3001.02
3002
3003
2113.02
2113.01
2113.03
2109.02
2109.01
2108.01
2108.02
2107
2112
2110
2111
2114
2131.02
2131.01
2151.01
2151.04
2151.03
2151.02
2132.01
2132.02
2150.01
2150.03
2150.02
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2161
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2153.01
2153.02
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2152.02
2152.01
2177.02
2177.01
2176
2175
2178.02
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2179.01
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2196
2197
2198
2199
2209
2210
2211
2208.01
2208.02
2208.03
2207.01
2207.02
2207.03
2200
2201
2202
2206.01
2206.02
2205
2203
2212.01
2212.02
2213.01
2213.02
EASTERN ST. LOUIS COUNTY

Figure 3. Strata for the medium exposure (1, 2, and 3) and low exposure strata (1', 2', and 3').

1. The whole high exposure area was counted and listed.
2. The total number of housing units actually found was divided by 3. This was the approximate size of each of the three minor strata.
3. Using a tract map along with the listing data, the three minor strata were formed as shown in Figure 2.

This stratification scheme defined nine unique strata. Two segments of approximately 50 housing units were selected from each minor stratum.

Selection of the First-Stage Sample--

For the medium and low exposure areas, sampling units were assigned to each stratum so that the sampling unit contained approximately 50 housing units. This was accomplished by dividing the stratum's total number of housing units by 50 then rounding to the nearest integer. The total number of sampling units assigned to each stratum is shown in Table 20. Each stratum's total sampling units were then distributed across the stratum's EDs and BGs based on the EDs or BGs total number of housing units. To accomplish this step, a list of all EDs and BGs in the stratum and their associated number of eligibles was prepared from 1970 census data. The housing units were then accumulated across this list so that each ED and BG had an accumulated number of housing units representing the sum of its total number of housing units and all housing units in EDs and BGs previous to it on the list. The accumulated number of housing units was divided by the expected number of housing units in the stratum, then rounded to the nearest integer to determine the accumulated number of sampling units. The number of sampling units assigned to each ED and BG was then determined by subtracting the EDs or BGs accumulated number of sampling units from the immediately preceding EDs or BGs accumulative sampling units. Any ED or BG that did not have enough housing units to be assigned one sampling unit was combined with other EDs or BGs in close geographic proximity until at least one sampling unit could be assigned to the combination. The two sampling units allocated to the stratum were then selected from all sampling units in the stratum with equal probabilities and without replacement. This was done by selecting two random numbers in the range from one to the total number of sampling units in the stratum.

For the high exposure area, the sample selection was essentially the same with the exception that the housing units were accumulated over the stratum. The accumulated number of housing units was divided by the number of housing units in the stratum, then rounded to the nearest integer to determine the accumulated number of sampling units. The two sampling units allocated to the stratum were then selected from all sampling units in the stratum with equal probabilities and without replacement. This was done by selecting two random numbers in the range from one to the total number of sampling units in the stratum.

Identification of Sampling Units Within EDs and BGs--

Recall that two random numbers were selected in the range from one to the total number of sampling units in the stratum, thus establishing a one-to-one correspondence between the sampling units and the random numbers.

Table 20. STRATUM HOUSING UNIT DATA AND SAMPLE ALLOCATION
ST. LOUIS, MO

High exposure				Medium exposure				Low exposure			
Stratum	Number of HUs	Number of SUs	Expected size of SU	Stratum	Number of HUs	Number of SUs	Expected size of SU	Stratum	Number of HUs	Number of SUs	Expected size of SU
1	593	12	49.42	1	151125	3023	49.99	1	26375	528	49.95
2	651	13	50.08	2	151215	3024	50.00	2	25854	517	50.01
3	615	12	51.25	3	149561	2991	50.00	3	26005	520	50.01
Total	1859	37	50.24	Total	451901	9038	50.00	Total	78234	1565	49.99

HU = Housing unit.
SU = Sampling unit.

Each random number, therefore, uniquely identified one sampling unit. Once the random number had been selected, it completely determined the selected sampling unit. The sampling unit then had to be located in an ED or BG defined in the 1970 census. If the sample fell partially or entirely within a BG or combination of BGs, then the location of the sampling unit was pinpointed using 1970 block statistics and their associated maps. If the sample fell within an ED or combination of EDs then the sampling unit was located using 1970 county ED maps.

When a selected sampling unit fell within a BG or combination of BGs, its location was determined and housing unit data for the individual blocks forming the BG were compiled. The total number of sampling units assigned to the BG was then distributed across the individual blocks based on their total housing units. Thus, if t was the total number of sampling units assigned to a selected BG and t_i was the number of sampling units assigned to block i within the selected BG, then $0 \le t_i < t$ and $\Sigma t_i = t$. Any block assigned $t_i = 0$ sampling units was combined with another block or blocks so that the combination had a positive number of sampling units. Any unit, single block or combination blocks, having a positive number of sampling units was called a segment with u sampling units. A sampling unit, k, within a segment, i, was defined as the cluster of housing units beginning with the kth housing unit in a list of housing units to be compiled by field personnel, $1 \le k \le u_i$, and then taking every u_ith housing unit thereafter. Thus, the random number identified the selected sampling unit located in a particular segment and determined the particular sampling unit within the segment by identifying it by a start number, k, and a rate $1/u_i$. The selected samples are shown in Table 21.

The selected first-stage sampling units in the medium and low exposure areas were counted and listed. The high exposure areas had been cruised and listed before the sample was selected. The actual housing unit counts are shown in Table 22.

Selection of the Second Stage Sample

Construction of the Second-Stage Frame--

The sampling frame at this stage was simply the list of all household members who met the criteria specified above and who agreed to participate in the survey.

Selection of the Second-Stage Sample--

The field supervisor was sent the screening questionnaires with the selected participant's household member number circled in red for each of the exposure areas (high, medium, and low). The sample for each segment was divided into two parts. The first part was made up of the blue screening questionnaires and the second part was made up of white copies of the blue screening questionnaires. The blue part was called the Sample and the white part was called the Supplementary Sample. The Samples and Supplementary Samples for all three exposure areas are listed in Table 23. The Sample was given to the field interviewer, while the Supplementary Sample was retained by the supervisor.

Table 21. SELECTED SAMPLES FOR ST. LOUIS, MO

Stratum	High exposure			Medium exposure				Low exposure			
	Number of HUs	Location (all in Madison County, IL)	Sampling unit	Number of HUs	Segment		Sampling unit	Number of HUs	Segment		Sampling unit
					Tract	BG/ED			Tract	BG/ED	
1	56	Bounded by Elm St., State Highway 111, and Maple Ave. in Roxanna	1/1-1	92	1122	102	1/2-2	53	2108.02	221,223	1/1-1
	55	Bounded by Central Ave., Thomas St., Chaffer Ave., and Tydeman Ave. in Roxanna	1/1-1	91	1171	304	1/2-1	56	2112	815	1/1-1
2	52	Bounded by town limits, Kindall Drive, and Big Bend Drive in Kendall Hills	1/1-1	43	2188	604,605 606	1/1-1	47	2114	318,319	1/1-1
	54	Bounded by Railroad, Maple St., Olive Road, East 1st St., Market St., and Hawthorne St. in Hartford.	1/1-1	49	2201	503,504	1/1-1	57	2152.02	103,104 105	1/1-1
3	55	Bounded by Doerr Ave., South 12th St., Esther Ave., 13th St., Chaffer Ave., and Thomas St. in Roxanna	1/1-1	57	1064	104	1/1-1	340	2212.02	114	1/6-4
	62	Bounded by Wood River Ave., East Lorena Ave., 2nd St., Ferguson Ave., 3rd St., and Madison Ave. in Roxanna	1/1-1	109	2106	105,106	1/2-1	58	2204.01	309	1/1-1

HU = Housing unit.

Table 22. HOUSING COUNTS PER SEGMENT FOR ST. LOUIS, MO

	High exposure		Medium exposure			Low exposure		
	No. housing units			No. housing units			No. housing units	
Stratum	Segment	Actual	Segment	70 census	Actual	Segment	70 census	Actual
1	31	56	21	53	33	11	46	31
	32	55	22	56	53	12	46	46
2	33	52	23	47	48	13	43	45
	34	54	24	57	86	14	49	51
3	35	56	25	57	86	15	57	56
	36	61	26	58	52	16	55	83

Table 23. SELECTED SAMPLES AND SUPPLEMENTARY SAMPLES FOR ST. LOUIS, MO

Sample			Supplementary sample		
Segment number	Housing unit number	Household member number	Housing unit number	Household member number	Selection order
		High exposure			
31	3	02	3	01	1
	16	02	39	02	2
	33	01	25	03	3
	34	01			
32	9	01	16	02	1
	43	01	43	02	2
	50	02	9	02	3
33	11	02	19	02	1
	17	01	39	01	2
	20	02	15	01	3
	26	02	35	02	4
	35	01	33	02	5
	43	01			
	43	02			
34	19	01	19	02	1
	37	01	41	02	2
	40	01			
	46	02			
35	9	02	5	01	1
	13	01	24	01	2
	13	02	36	02	3
	39	02	53	01	4
	43	01	43	02	5
36	61	02	--	--	-
		Medium exposure			
11	20	02	40	01	1
	44	03			
12	17	01	17	02	1
	43	01	27	01	2
	65	01	35	02	3
			35	01	4

(continued)

Table 23 (continued)

Sample			Supplementary sample		
Segment number	Housing unit number	Household member number	Housing unit number	Household member number	Selection order
13	22	01	4	02	1
	33	02	22	02	2
14	8	02	23	01	1
	44	01	43	02	2
15	2	02	14	01	1
	9	03	22	01	2
	22	02	6	02	3
	34	01	9	02	4
	45	01	51	02	5
	52	02	1	01	6
	56	01	54	01	7
			51	01	8
16	12	03	52	02	1
	18	02	10	03	2
	20	02	128	02	3
	22	02	60	01	4
	32	02	72	02	5
	38	01	58	01	6
	60	02	56	01	7
	72	01	138	02	8
	156	01	92	02	9
		Low exposure			
21	2	01	5	01	1
	4	01	10	02	2
	7	01	33	01	3
	10	01	6	01	4
	19	01	33	02	5
	32	02	9	01	6
			9	02	7
			32	01	8
			25	02	9
22	20	01	--	--	-

(continued)

Table 23 (continued)

Sample			Supplementary sample		
Segment number	Housing unit number	Household member number	Housing unit number	Household member number	Selection order
23	24	03	22	01	1
	35	03	25	01	2
	35	04	47	01	3
	37	02	31	02	4
	39	02	46	02	5
	42	03	29	01	6
	47	02	1	02	7
			39	01	8
			46	01	9
			2	01	10
			18	02	11
24	46	01	52	02	1
	48	01	1	02	2
	48	02	62	01	3
	50	01	46	02	4
	64	01	70	02	5
	70	01	54	02	6
			34	01	7
			6	02	8
			68	02	9
			50	02	10
25	90	02	44	02	1
	94	01	2	01	2
			96	02	3
			94	01	4
26	15	01	10	02	1
	15	02	26	03	2
	38	01	12	01	3
			33	02	4
			38	02	5

In the field, the eligible persons listed in the Sample were contacted in any order. Every effort was made to get these people to participate. After all procedures had been exhausted and still k, say, refused to participate, then the supervisor selected the first k people from the Supplementary Sample. These k people were then contacted to see if they would participate. Again, if p of these would not participate, then the supervisor selected the next p from the Supplementary Sample. This procedure was continued until the required number of people from the segment agreed to participate.

After the required number of people agreed to participate, the interviewer continued contacting people from the Supplementary Sample until one more than was required agreed to participate. The number of people contacted to get the number was recorded. The last person was not part of the survey; however, if a member of the panel dropped out the last person was made part of the panel. If this happened, the interviewer continued to contact people from the Supplementary Sample until one more than was required agreed to participate, then the number contacted was updated. The interviewer was required to contact this extra person to fulfill the requirements of sequential without replacement sampling (see Appendix C). The sample sizes are shown in Table 24.

Calculation of Sampling Weights

The selection procedure of the second stage unit (i.e., the sample of eligible persons) described above is called Inverse Sampling (See Appendix C). This leads to the Negative Hypergeometric distribution. Using the properties of this Negative Hypergeometric distribution, the sampling weights were estimated.

For convenience, the notation used in this section is summarized below:

h = 1, 2, 3 indexes the minor stratum cells.

i = indexes the first-stage units; values of i are nested within h.

N(h) = the number of first-stage units, cluster of housing units called segments, in the h-th stratum.

n(h) = the number of first-stage units, segments, selected from the h-th stratum (2).

N(hi) = the number of eligible persons who agreed to participate at the time of screening in the (hi)-th first stage unit, segment

n(hi) = the number of eligible persons who participated from the (hi)-th segment

p(hi) = one less than the number contacted to get one more than needed to agree to participate in the (hi)-th segment

Table 24. SAMPLE SIZES OF ELIGIBLE PERSONS

	High exposure				Medium exposure				Low exposure			
		Eligibles				Eligibles				Eligibles		
Stratum	Segment	Total	Selected	Responded	Segment	Total	Selected	Responded	Segment	Total	Selected	Responded
1	31	9	5	5	11	3	2	2	21	15	14	5
	32	6	4	3	12	7	6	2	22	1	1	0
2	33	12	8	7	13	4	3	2	23	18	7	7
	34	6	4	4	14	4	3	2	24	16	10	6
3	35	10	0	6	15	15	14	4	25	6	3	2
	36	1	1	0	16	18	17	8	26	8	7	3
	Total	44	22	25	Total	51	45	20	Total	64	42	23

An unbiased estimate of the sampling weight for an eligible person is given by

$$w(hij) = \frac{N(h)}{2} \; \frac{N(hi)}{p(hi)}$$

for all

$$i = 1, 2, \ldots, n(hi)$$

eligible persons who participated in the (hi)-th segment. The sample weights are shown in Table 25.

Nonresponse Adjustment

A nonresponse compensation was made by using p(hi) based on the number of eligible persons who participated in the weight calculations. This is the same as using the average value of the response variable of the responding eligible persons for the nonrespondents in the same segment.

Table 25. SAMPLE WEIGHTS FOR ST. LOUIS, MO

City	Exposure	Stratum	Segment	N(h)	n(h)	N(hi)	p(hi)	Weight
			High exposure					
2	1	1	31	12	2	9	5	10.800
2	1	1	32	12	2	6	4	9.000
2	1	2	33	13	2	12	8	9.750
2	1	2	34	13	2	6	4	9.750
2	1	3	35	12	2	10	9	6.667
2	1	3	36	12	2	1	-	--
			Medium exposure					
2	2	1	11	3023	2	3	2	2267.250
2	2	1	12	3023	2	7	6	1763.417
2	2	2	13	3024	2	4	3	2016.000
2	2	2	14	3024	2	4	3	2016.000
2	2	3	15	2991	2	15	14	1602.321
2	2	3	16	2991	2	18	17	1583.471
			Low exposure					
2	3	1	21	528	2	15	14	282.857
2	3	1	22	528	2	1	-	--
2	3	2	23	517	2	18	7	664.714
2	3	2	24	517	2	16	10	413.600
2	3	3	25	520	2	6	3	520.000
2	3	3	26	520	2	8	7	297.143

SECTION 7

FIELD OPERATIONS

GENERAL PRINCIPLES

The Survey Operations Center (SOC) was responsible for the conduct of all field activities. This included development of data collection instruments; recruiting and training of field staff; supervision of actual data collection; and receipt, editing, and preparation of data for entry and conversion to machine-readable form. These activities were the basis of SOC involvement at the two data collection sites, Houston, TX, and St. Louis, MO. Field operations consisted of several steps leading to the sample selection and actual data collection. These included "counting and listing" the selected sample areas and screening households for eligible individuals. The sample, composed of eligible individuals who expressed willingness to participate, was recontacted, the questionnaires administered, and appointments made to collect the biological samples. At each site, appropriate contacts were made with local health officials and EPA regional offices to garner support for the activities. Public relations contacts were made through local officials.

DEVELOPMENT OF DATA COLLECTION INSTRUMENTS

Appendix D of this report contains copies of the household data collection instruments developed for this study. These instruments and supporting information and rationale (also included in Appendix D) were provided to EPA's Office of Pesticides and Toxic Substances for the submission to OMB for clearance to execute the study. While OMB approval was being obtained, several pretest activities were conducted to validate methodology. Two data forms were developed. The first, a Household Screening Questionnaire (HSQ), was constructed to assist in the development of the sampling frame by providing a complete list of household residents that indicated their eligibility and willingness to participate. The matrix in Question 10 provided the major input on eligibility by displaying age, smoking status, health status, and vocational or avocational exposure to benzene. Information collected on the HSQ was summarized on a Household Screening Log (HSL) created to summarize each segment of each stratum at each site. A study questionnaire was developed to obtain demographic, occupational, and household information, as well as the pertinent data on the samples that were collected. Participant Consent Forms were developed and specifically prepared for each stratum and each site. For each site, the appropriate local officials were listed as contact persons. The high exposure area consent form reflected the need for a blood sample and the concomitant larger incentive.

RECRUITING AND TRAINING OF FIELD INTERVIEWERS

RTI has a staff of field supervisors available in several sites across the country. St. Louis and Houston, the study sites, are the home areas for two of the supervisors. These supervisors were responsible for recruiting and retraining interviewers for the study. In addition, the supervisors assisted the Survey Director in training the interviewers. Two training sessions were held at each site. The first was a general introduction to RTI and the study and specific details of the screening procedure. The second training session was held during the break between screening and the administration of the study questionnaire. This second training focused on the study questionnaire and how the interviewers were to assist in the scheduling and collection of biological samples. This training involved the chemistry group's field staff and the phlebotomist (nurse or medical technologist trained in collecting blood samples) from the health department in the high exposure area.

Throughout the screening process and the administration of the study questionnaire, the field supervisor maintained day-to-day contact with the interviewers and provided guidance, coordination, and problem resolution. The RTI Survey Director maintained contact with the supervisors. All forms were examined by the supervisors for quality control and then sent to RTI for processing.

DATA COLLECTION

In both the Houston and St. Louis area sites, the field data collection processes consisted of several steps. Areas chosen, as described in Section 6, were "counted and listed" by the Field Supervisors. This process consisted of identifying an area by its boundaries and then driving or walking through the area in a specified replicable manner and listing the address or identifying description of each apparent housing unit. These segment listings were examined for any necessary subsampling and became the basis for screening. Each selected housing unit was approached and the screening questionnaire was administered to any adult resident. Housing units were visited repeatedly until the unit was interviewed, determined to be vacant, or no response was obtained after multiple visits.

Based on the data collected, a sample of eligible persons who were willing to participate was chosen. The field interviewers then returned to the field, and recontacted the selected individuals. At the time of this contact, the interviewer provided a more complete description of the study, had the participant sign the consent form, administered the study questionnaire, collected the tapwater samples, and set up an appointment for the air monitor to be installed. A second appointment, the morning after the monitor was positioned, was made to retrieve the monitor and collect the breath sample and, in the high exposure areas, the blood sample.

Houston

Field activities were executed first in Houston. Based on the experience gained, the St. Louis activities were planned for and accomplished in a more effective manner. January 1979 marked the start of activities. Segment maps were sent to the field supervisor for the "counting and listing." This activity was slow due to the rapid growth of the area, but was completed in February. Interviewers were recruited and hired during late February so that the screening activities could be started in March. By the March 19 training date, sampling of strata for screening was 80 percent completed. During the last two weeks of March the remaining sampling was finished and all areas screened. Household data collection began in early April as the samples were selected. The Houston Health Department provided a phlebotomist who began work in the high exposure areas in mid-April. By the end of April, only 45 air and breath samples had been collected and by the end of the field collection period on May 5, a total of 50 samples had been collected and 50 questionnaires administered. Several problems were related to the difficulties in data collection. As alluded to before, the size and rate of growth of the area was not considered when the strata and sample segments were selected. The travel time between strata precluded working in more than one area in any one day, and indeed the travel to and from areas was often extremely long. Based on this experience, the selection of strata and segments in St. Louis was reconsidered and the number of sample areas reduced.

A second problem, which was partially overcome, was the change in eligibility status of selected individuals between screening and actual data collection. Persons started smoking, became ill, or now had exposure to benzene from a new job or from activities around the home (e.g., painting, gardening, or hobbies). In St. Louis this problem was partially alleviated by reducing the time between screening and final data collection. However, some changes in eligibility were due to improper reporting during the screening interview. This source of error is beyond the control of the field staff. Some percentage of over-sampling could relieve this problem as well as the problem of persons no longer willing to participate.

St. Louis

The timetable of activities was shorter in St. Louis than in Houston. The "counting and listing" that started in late June was followed in July by hiring of interviewers. They were trained and started the screening in August. The sample was drawn and data collection was started with the second training session in early September. All three sample areas were finished in early October. The response rate was higher in St. Louis as was the ease of data collection. The interviewers were told to schedule appointments at specific intervals that allowed for equipment management and transport. In addition, appointments were grouped in areas on specified days. For example, early field efforts were concentrated in the high exposure area. Four days out of six were designated for data collection in the high area. After this area was completed, three days a week were spent in the medium and low exposure areas. Monday, Tuesday, and Wednesday were designated for low areas during one week and for medium areas the next. This made planning and executing data collection much simpler and allowed for ease of coordination with the phlebotomist from the regional office of the Illinois Department of Health. These problem areas and their potential resolution will be of great assistance in future body-burden studies.

DATA RECEIPT AND PREPARATION

As data were received, the questionnaires were logged in and were subjected to a manual review for completeness. This review, by the Survey Director, was followed by an edit and range check. After problems were resolved, the data were converted to machine readable form and a data tape was prepared for use in the analysis. The only data entered were from the study questionnaire and the results of the analyses of samples. The two data sets were linked by the study number generated on a series of labels and attached to all paperwork and samples. This mechanism works extremely well in studies requiring multiple questionnaires and multiple sample types or replicates.

SECTION 8

SAMPLE COLLECTION AND CHEMICAL ANALYSIS

The methods developed for the pretest of filling station attendants and tank truck drivers were used for the sample collection and chemical analysis for the two study sites. Some modifications were required to meet the logistical problems of field sampling. The sampling and chemical analysis protocols are given in Appendix A with the modifications indicated below.

SAMPLE COLLECTION METHODOLOGY

Blood Collection

Because of technical difficulties associated with sterilization of glass syringes in the field, an alternative collection method for blood was evaluated. Venoject tubes (Kimble), which are designed for use with gas chromatography, were evaluated for their suitability for collecting blood samples for benzene analysis. Three nonsmoker laboratory workers with no known benzene exposure were used as donors for the evaluation. Each sample was analyzed in replicate. No detectable benzene was found for any of these individuals. The limit of detection was 0.1 ng/mL for all but two injections were it was ∿1 ng/mL due to an interferent peak. Replicate injections did not show the same peaks hence they were presumed to be an artifact of those particular injections. Therefore the Venoject tubes were used for the blood collection.

Breath Collection - (Mobile Van)

As indicated in Section 6, the block groups contained two to six participants and were, for the most part, widely distributed. To sample this population effectively, the sampling team had to have considerable mobility. To sample a sufficient number of participants, at least two of these block groups had to be sampled each day. To accomplish this goal the sampling equipment was set up in a van. The primary concern with this approach, as the contamination of samples with benzene from auto exhaust in and about the van, was circumvented by placing all parts of the sampling apparatus that would be subject to contamination in glove bag(s) under a slight positive pressure of helium (hydrocarbon free). This excluded the majority of contaminated air from the sampling medium and the exterior surfaces of the cartridges.

SAMPLE CHEMICAL ANALYSIS--HOUSTON, TX

The chemical analyses of the sample collected in the Harris County, TX, study are summarized in Table 26 along with the pertinent meteorological data. The meteorological data cover the period of the air sampling. It should be noted, however, that the air samples were collected inside the participant's home. The locations of the various segments are presented in Figures 4 through 6. The segment designations are: 10-19, high exposure group; 20-29, medium exposure group; and 30-39, low exposure group.

The control and blank data for air, breath, and water samples are given in Table 27. The blank values showed a very high time-dependence. Blank values were plotted against time and the breath samples corrected according to the analysis date. Since sampling and analysis chronologies were parallel, the samples were corrected by the blanks that shared the closest chronology to the samples.

Considerable difficulty was encountered with the blood analysis. Detection limits that had been on the order of 1 ng/mL for the pretest could not be duplicated for the samples collected in the field, shipped to the laboratory, and stored for more than a month. The primary problem was one of interference in the GC/FID procedure because of large amounts of other hydrocarbons. An attempt to improve the selectivity of the method by using a photoionization detector, which detects aromatic compounds selectively, was made. The sensitivity, however, was not adequate to detect the ∿20 pg of benzene that would have been introduced from a 1-ng/mL sample. In fact, the limit of detection was 20 ng/mL, approximately that found in current literature (34). Several steps were taken to minimize the problems encountered with the blood analysis between the two study sites. In the St. Louis study, the blood was collected during the first period of the study, flown back to the laboratory and analyzed. The blood samples were the first analyzed to avoid contamination that might occur during storage. The use of glass capillary gas chromatography increased the sensitivity and reduced interferences. A limit of detection of less than 1 ng/mL was obtained with the GC/FID technique.

SAMPLE CHEMICAL ANALYSIS--ST. LOUIS

The sample chemical analysis results for the samples collected in the St. Louis, MO-Wood River/Roxana/Hartford, IL, study are summarized in Table 28 along with the pertinent meteorological data. The meteorological data cover the period of the air sampling. The air samples were collected in the participant's homes. The locations of the various segments are presented in Figures 7 through 9. The segment designations are: 30-36, high exposure group; 20-26, medium exposure group; and 10-16 low exposure group.

Three breath samples were confirmed using GC/MS/COMP. For two of these, the replicate sample was analyzed by GC/FID and the results are presented in Table 29.

Table 26. BENZENE LEVELS FOUND IN THE HOUSTON STUDY 4/3/79-5/5/79

			Benzene levels				Meteorology		
								Wind	
Date	Subject no.	Segment	Air ($\mu g/m^3$)	Breath ($\mu g/m^3$)	Water ($\mu g/L$)	Blood ($\mu g/L$)	Temp. (°C)	Speed (kn)	Direction
4/3,4/79	10231	25	12	4.8	<1	-[b]	13-17	6-9	35
4/3,4/79	10827	22	10	-[a]	<1	-			
4/3,4/79	10835	22	20	1.8	<1	-			
4/3,4/79	10876	21	26	2.5	<1	-			
4/5,6/79	10819	20	33	2.4	<1	-	7-22	0-9	13-16
4/5,6/79	10843	23	25	4.4	<1	-			
4/7,8/79	10850	26	10	1.0	<1	-	20-21	4-8RF	15
4/7,8/79	10223	26	10	1.3	<1	-			
4/10,11/79	10496	36	4.5	-[a]	<2	-	22-23	9-16F	15
4/9,10/79	10207	36	3.4	2.9	<2	-	18-20	5-10F	10
4/11,12/79	10488	32	27	4.0	<2	-	20-28	7-11	SF(10 16 34)
4/11,12/79	10479	32	9	1.7	<1	-			
4/12,13/79	10983	27	8.0	-[a]	<1	-	22-27	5-10	F(08)14(27)
4/12,13/79	11007	27	2.0	2.0	<1	-			
4/12,13/79	10991	37	13	-[a]	<1	-			
4/13,14/79	10583	32	18	1.4	<1	-	12-26	5-8	36
4/13,14/79	10520	32	17	0.7	<2	-			
4/15,16/79	10462	32	13	1.9	3	-	18-27	5-12F	09
4/16,17/79	10603	24	4.4	2.7	<1	-	19-24	6-10	10

(continued)

Table 26 (continued)

Date	Subject no.	Segment	Benzene levels				Meteorology		
								Wind	
			Air ($\mu g/m^3$)	Breath ($\mu g/m^3$)	Water ($\mu g/L$)	Blood ($\mu g/L$)	Temp. (°C)	Speed (kn)	Direction
4/16,17/79	10199	24	11	2.0	<1	-			
4/18,19/79	10751	12	13	3.0	<1	<20	18-19	5-12F	08-15
4/18,19/79	10702	15	11	-[a]	<1	<20			
4/19,20/79	10678	17	18	3.5	<1	<20	19-22	2-9TRF	09
4/20,21/79	10744	11	-[b]	0.8	<1	<20			
4/20,21/79	10769	17	6.7	ND[c]	<1	<20	17-19	3-6F	36
4/20,21/79	10710	17	6.7	1.4	<1	<20			
4/20,21/79	10652	11	8.6	2.8	<2	<20			
4/22,23/79	10629	15	6.1	3.5	<1	-[d]	17-20	5-8F	30
4/22,23/79	10694	17	3.1	14	<1	<20			
4/22,23/79	10660	11	5.2	1.7	<2	<20			
4/22,23/79	10611	12	31	5.6	<1	<20			
4/22,23/79	10637	11	32	9.0	<1	<20			
4/23,24/79	10728	19	35	ND[b]	<1.0	-[d]	13-23	0-5F	07-34
4/23,24/79	10645	11	16	3.1	<1	<20			
4/24,25/79	10595	12	14[e]	5.1	<1	<20	15-27	0-10	16-29
4/24,25/79	10793	12	≤14[e]	8.6	<1	<20			
4/25,26/79	10439	25	3.1	3.8	<1	-	19-27	5-10	18
4/25,26/79	10132	21	4.6	2.3	<1	-			

(continued)

Table 26 (continued)

Date	Subject no.	Segment	Benzene levels				Meteorology		
								Wind	
			Air ($\mu g/m^3$)	Breath ($\mu g/m^3$)	Water ($\mu g/L$)	Blood ($\mu g/L$)	Temp. (°C)	Speed (kn)	Direction
4/25/26/79	10165	21	11	2.0	1	-			
4/27,28/79	10447	35	5.6	8.2	1	-	12-26	4-9	(13) 02
4/27,28/79	10454	30	4.0	2.0	1	-			
4/27,28/79	10074	30	21	0.3	1	-			
4/29,30/79	10033	27	30	1.0	1	-	15-22	4-9	06
4/30,5/1/79	10090	29	25	4.1	1	-	16-24	3-10FS	(13) 9 (3)
4/30,5/1/79	10082	22	45	1.0	1	-	22-24	7-10	13
5/2,3/79	10272	33	18	0.4	1	-			
5/2,3/79	10066	33	18	7.5	1	-			
5/3,4/79	10041	34	17	ND	1	-	18-27	4-13TR	16,32
5/4,5/79	10256	33	4.3	-[a]	1	-	13-16	5-10	34
5/4,5/79	10371	33	9.8	-[a]	1	-			

[a] Subject did not breathe into apparatus correctly.

[b] Not detected above apparatus blank.

[c] Sample lost.

[d] Not analyzed.

[e] Interference peaks on the chromatogram.

Meteorology Key:

R = Rain
F = Fog
T = Thunderstorm
S = Smoke

Wind Key:

Directions are those from which wind blows. Indicated in tens of degrees from the north: i.e., 09 for east, 18 for south, 27 for west. Entry of 00 in the direction column indicates calm.

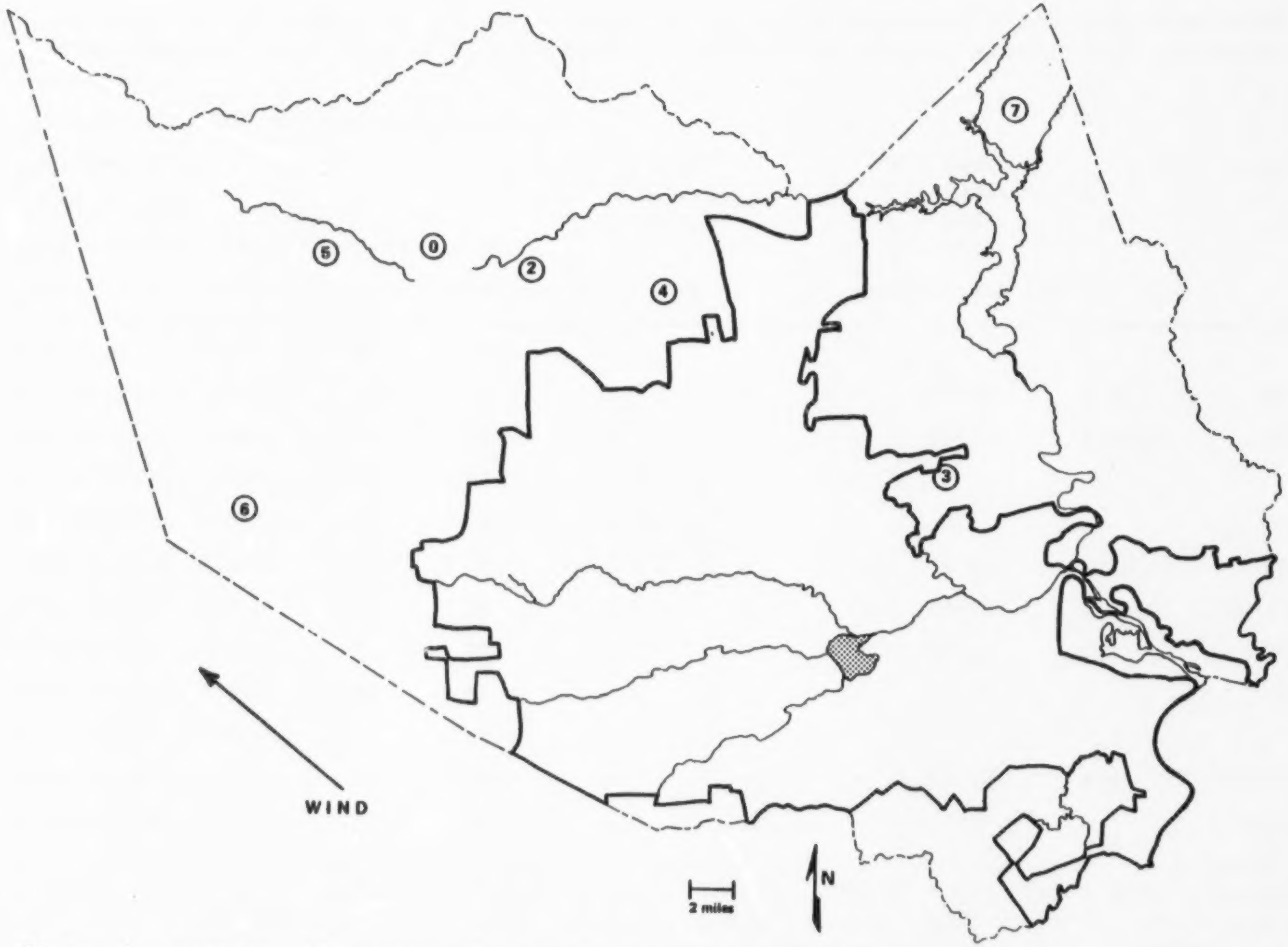
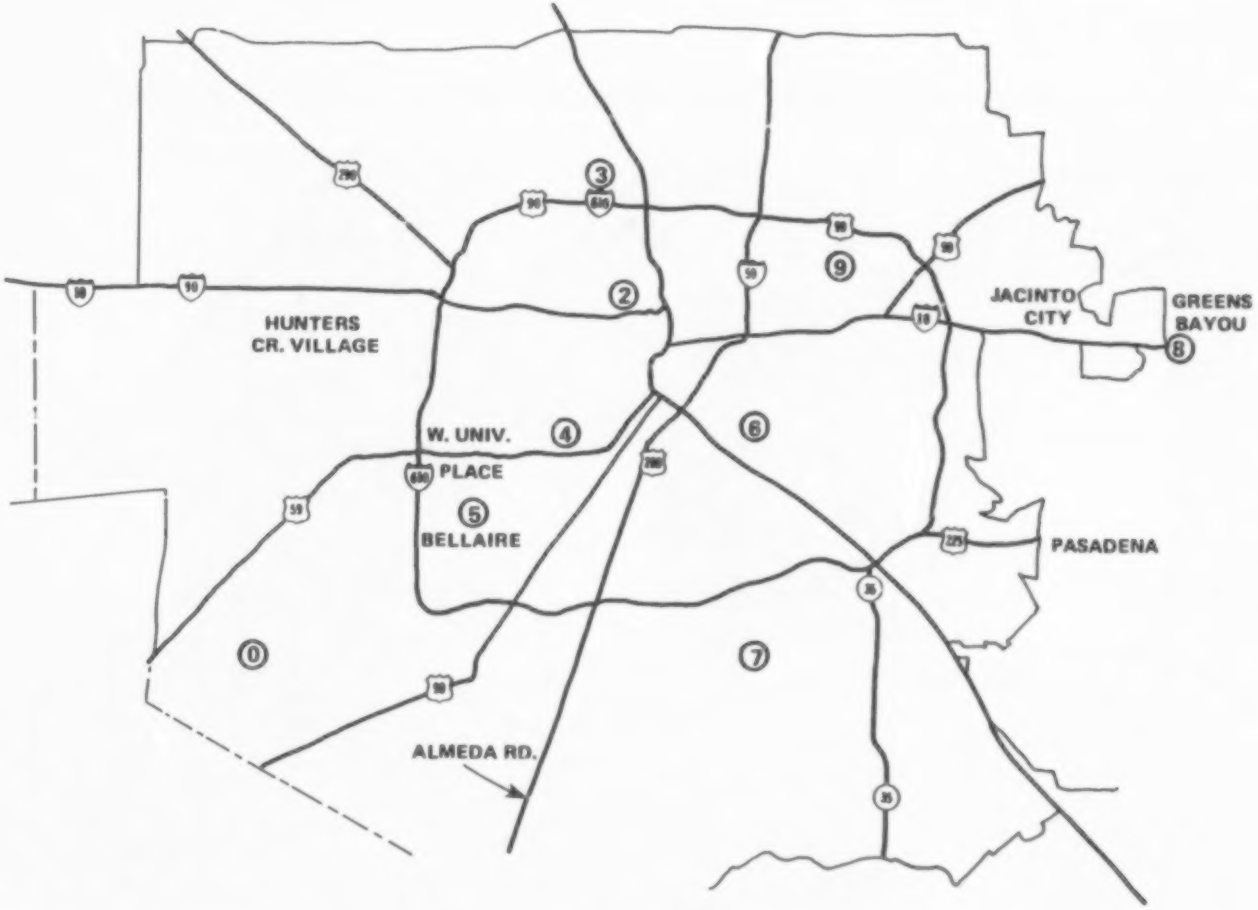
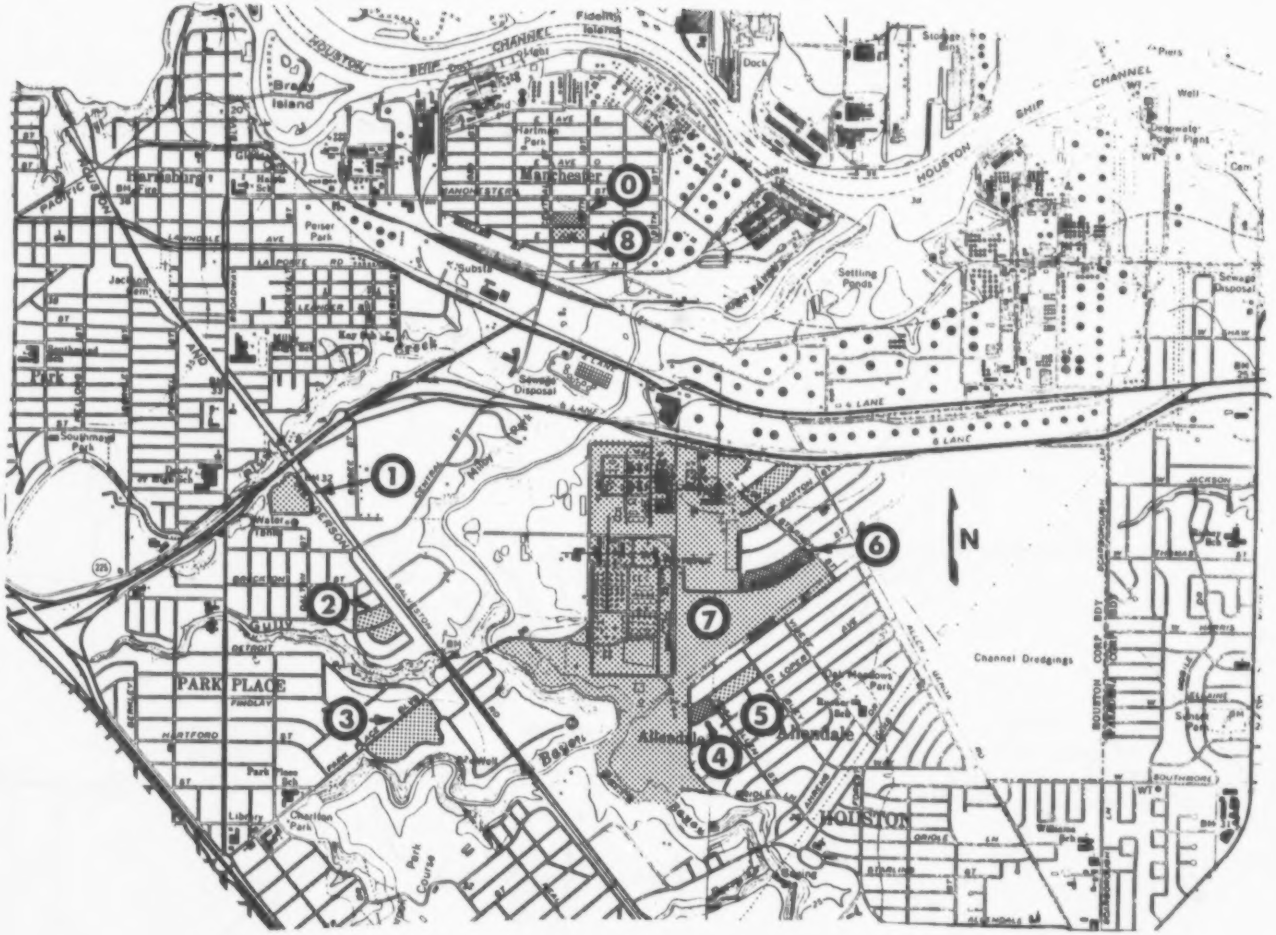

⑦
⑤
⓪
②
④
③
⑥
WIND
2 miles
N

Figure 4. Location of segments for the low exposure sample in Harris County, TX; shaded area is high exposure area; Houston City limits = bold line.



③
②
⑨
HUNTERS
CR. VILLAGE
JACINTO
CITY
GREENS
BAYOU
⑧
W. UNIV.
④
⑥
PLACE
⑤
BELLAIRE
PASADENA
⓪
⑦
ALMEDA RD.
290
90
610
10
59
288
225
35

Figure 5. Location of segments for the medium exposure sample in Houston, TX.



0
1
2
3
4
5
6
7
8
N
HOUSTON SHIP CHANNEL
Brady Island
Fidelity Island
Harrisburg
Manchester
Hartman Park
Settling Ponds
Sewage Disposal
Channel Dredgings
PARK PLACE
Allendale
Park
HOUSTON
Southmayd Park
Jackson Cem
Mason Park

Figure 6. Location of segments for the high exposure sample in Houston, TX.

Table 27. QUALITY CONTROL DATA FOR HOUSTON STUDY

Media	Date analyzed	Sample	Benzene (ng)	% Recovery
Air	5/14/79	Field Blank 1	18	
		Field Control 1	814	80
	6/1/79	Laboratory Blank	28	
		Laboratory Control	Lost	
	6/19/79	Field Bank 2	97	
		Field Control 2	600	50
Breath	6/6/79 (4/14/79)[a]	Field Blank 1	11	
	(4/22/79)[a]	Field Blank 2	39	
	(4/22/79)[a]	Field Control 1	806	81
	6/13/79 (4/22/79)[a]	Field Control 1	680	68
	6/21/79 (4/26/79)[a]	Field Blank 3	56	
	7/3/79 (5/5/79)[a]	Field Blank 4	122	
	(5/5/79)[a]	Field Control 2	1300	130
	(5/14/79)[a]	Laboratory Blank	70	
	(5/14/79)[a]	Laboratory Control	800	80
Water	7/18/79	Field Blank 1[b]	<1 μg/L	
		Field Control 1[b]	11 μg/L	110
		Field Blank 2[b]	<1 μg/L	
		Field Control 2[c]	27 μg/L	270

[a] Refers to date control or blank was collected on the spirometer.

[b] Prepared in the laboratory before the sampling trip.

[c] Prepared in the field on 4/14/79.

Table 28. BENZENE LEVELS FOUND IN THE ST. LOUIS STUDY 9/18/79-10/20/79

			Benzene levels				Meteorology		
								Wind	
Date	Subject No.	Segment	Air ($\mu g/m^3$)	Breath ($\mu g/m^3$)	Water ($\mu g/L$)	Blood ($\mu g/L$)	Temp. (°C)	Speed (kn)	Direction
9/18,19/79	20537	21	17	1.1	ND	-	13-29	0-10	H 35 (8)
	20586	21	22	2.2	ND	-			
	20552	21	32	11	ND	-			
9/19,20/79	20024	16	20	2.3	ND	-	16-26	4-12	H 12
	20032	16	19	7.0	ND	-			
	20040	16	18	3.8	ND	-			
	20057	16	22	4.0	ND	-			
9/20,21/79	20347	34	19	12.0	ND	-	14-24	3-9	H 16 (8V) 35
	20362	34	-[a]	6.2	ND	-			
	20388	34	18	4.5	ND	ND			
9/21,22/79	20420	35	6.2	8.9	ND	-	11-18	3-12	35
	20412	35	6.2	-[a]	ND	ND			
	20511	35	23	3.8	ND	ND			
9/23,24/79	20404	35	11	3.0	ND	-	10-22	0-6	HF 12 (calm)
	20370	32	-[a]	7.3	ND	-			
	20396	32	14	3.5	ND	-			
9/24,25/79	20339	31	86	16	ND	-	16-25	0-7	H 13 calm 22
	20321	31	86	9.2	ND	ND			
	20909	31	25	4.6	ND	ND			
	20354	31	17	9.2	ND	ND			

(continued)

Table 28 (continued)

Date	Subject No.	Segment	Benzene levels				Meteorology		
			Air (μg/m³)	Breath (μg/m³)	Water (μg/L)	Blood (μg/L)	Temp. (°C)	Wind	
								Speed (kn)	Direction
9/26,27/79	20446	31	17	4.2	ND	ND	15-28	0-10	HF 16 (calm) 12
	20438	35	17	7.7	ND	ND			
	20503	32	17	7.7	ND	ND			
9/27,28/79	20297	33	35	-[a]	ND	ND	14-28	0-9	HF 16 (calm) 22
	20271	33	3.7	4.1	ND	ND			
	20917	33	3.8	6.5	ND	ND			
	20891	33	3.8	2.1	ND	-			
	20305	33	25	4.7	ND	ND			
9/28,29/79	20313	33	6.6	2.8	ND	ND	19-28	3-11	H 17-25
	20453	35	52	7.7	ND	ND			
10/1,2/79	20461	33	17	5.7	ND	ND	14-23	14-23	31
	20479	34	18	2.5	ND	ND			
10/2,3/79	20594	26	3.9	2.6	ND	-	11-21	0-10	H 15V
	20545	26	3.9	5.2	ND	-			
10/3,4/79	20610	13	4.0	-[b]	ND	-	8-16	6-10	27
	20560	25	9.9	5.1	ND	-			
	20602	13	13	7.0	ND	-			
10/4,5/79	20099	16	-[b]	-[b]	ND	-	4-15	4-14	F 28
	20073	16	10	-[b]	ND	-			
	20081	16	6.7	-[b]	ND	-			

(continued)

Table 28 (continued)

			Benzene levels				Meteorology		
								Wind	
Date	Subject No.	Segment	Air (μg/m³)	Breath (μg/m³)	Water (μg/L)	Blood (μg/L)	Temp. (°C)	Speed (kn)	Direction
10/5,6/79	20115	23	10	-[b]	ND	-	12-19	8-20 (G25)	19-28
	20149	23	30	-[b]	ND	-			
	20131	23	30	11	ND	-			
	20107	23	44	-[b]	ND	-			
	20123	23	46	4.9	ND	-			
10/8,9/79	20628	24	4.2	5.0	ND	-	8-31	7-22 (G26)	R33
	20644	24	4.2	17	ND	-			
	20651	24	3.4	-[b]	-	-			
	20669	24	118	8.8	-	-			
	20636	14	125	26	ND	-			
10/9,10/79	20156	23	-[b]	-[b]	ND	-	3-12	3-16	29-26
	20164	23	-[b]	1.4	ND	-			
10/10,11/79	20172	15	5.1	9.4	ND	-	12-14	9-18 (G25)	18-25
10/11,12/79	20214	15	-[b]	3.1	ND	-	15-23	9-19	32 (calm) 26V
	20198	15	-[b]	2.3	ND	-			
	20206	11	-[b]	-[b]	ND	-			
10/12,13/79	20677	25	43	-[b]	ND	-	1-12	6-17	32
	20693	21	-[b]	5.5	ND	-			
10/17,18/79	20248	12	-[b]	14	ND	-	13-18	0-11	12 (calm) 12
	20230	12	-[b]	19	ND	-			
	20222	16	-[b]	9.4	ND	-			

(continued)

Table 28 (continued)

Date	Subject No.	Segment	Benzene levels				Meteorology		
								Wind	
			Air ($\mu g/m^3$)	Breath ($\mu g/m^3$)	Water ($\mu g/L$)	Blood ($\mu g/L$)	Temp. (°C)	Speed (kn)	Direction
10/18,19/79	20578	26	6.3	18	ND	-	17-23	7-15 (G23)	F16, 30, 21
	20719	14	-[b]	4.4	ND	-			
	20735	24	-[b]	9.3	-	-			
	20727	24	-[b]	6.1	ND	-			
10/19,20/79	20685	21	9.1	6.2	ND	-	22-25	12-17 (G23)	H 17
10/20,21/79	20834	15	3.5	11	ND	-	22-25	18-19 (G33)	18
	20255	11	7.4	7.0	ND	-			

[a] Sample containers damaged in transit.

[b] Chromatographic interferences prevented quantitation.

Meteorology Key:
R = Rain
F = Fog
T = Thunderstorm
S = Smoke

Wind Key:

Directions are those from which wind blows. Indicated in tens of degrees from the north: i.e., 09 for east, 18 for south, 27 for west. Entry of 00 in the direction of column indicates calm.

ND = not detected.

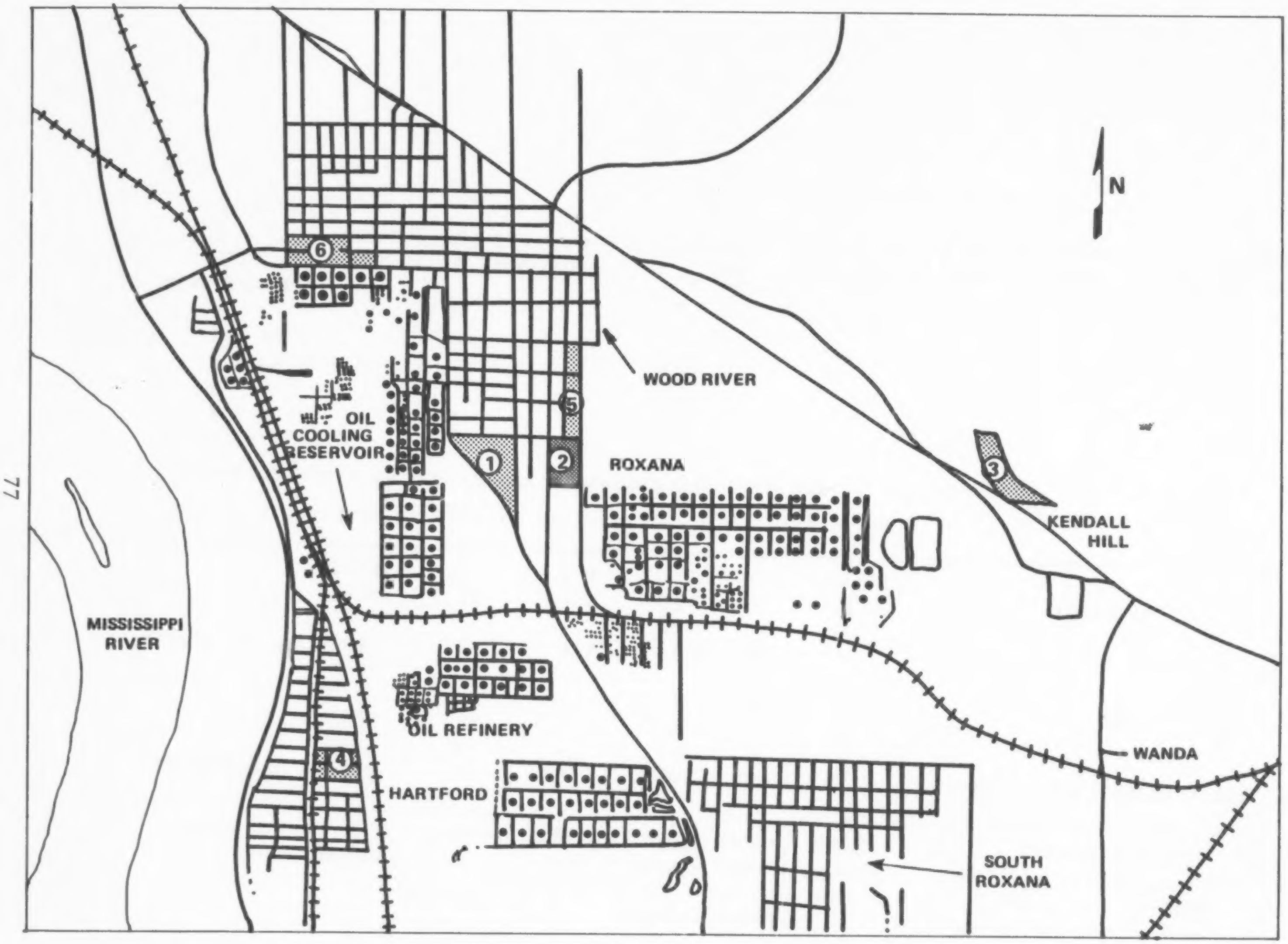

N
WOOD RIVER
ROXANA
KENDALL HILL
OIL COOLING RESERVOIR
MISSISSIPPI RIVER
OIL REFINERY
HARTFORD
WANDA
SOUTH ROXANA
1
2
3
4
5
6

Figure 7. Location of segments for the high exposure sample in Wood River/Roxana/Hartford, IL (St. Louis study).

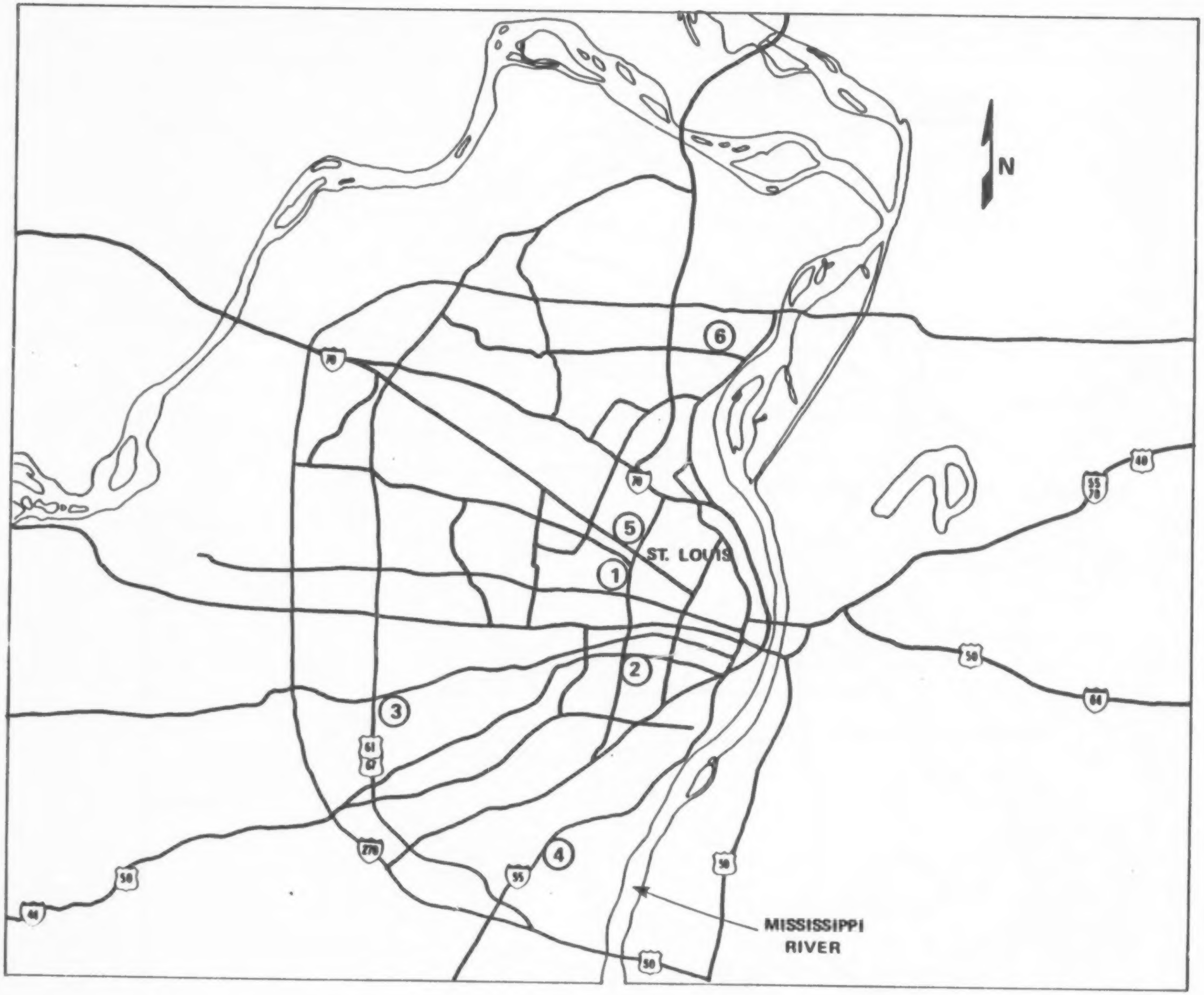

N
70
70
40
55
70
6
5
ST. LOUIS
1
2
3
61
67
50
64
270
55
4
50
50
44
50
MISSISSIPPI
RIVER

Figure 8. Location of segments for medium exposure sample in St. Louis, MO.

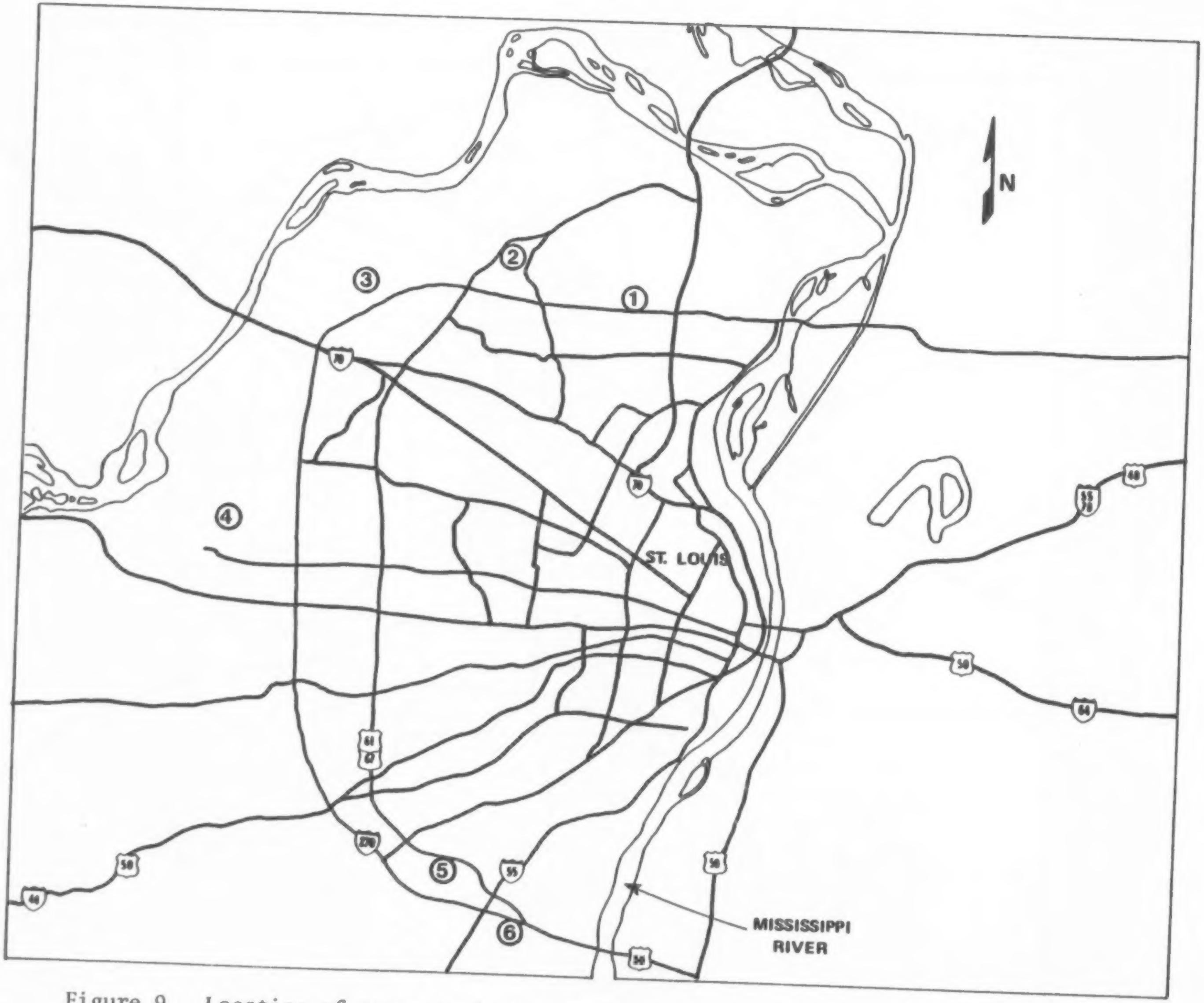

N
①
②
③
④
⑤
⑥
ST. LOUIS
MISSISSIPPI RIVER
70
70
40
55 70
50
64
61 67
270
55
50
50
44

Figure 9. Location of segments in the low exposure area in St. Louis, MO.

Table 29. CONFIRMATION BY GAS CHROMATOGRAPHY/MASS SPECTROMETRY

Benzene found in replicate breath samples by		
GC/FID ($\mu g/m^3$)	GC/MS ($\mu g/m^3$)	Ratio GC/FID:GC/MS
7.8	15.4	0.50
lost	8.9	-
15.6	15.8	0.99
	Mean	0.74

Analysis of the blank and control samples for each of the media are presented in Table 30. Breath blank samples showed higher than usual benzene values. Excluding those showing obvious interferences, the average was 4.2 ± 1.9 μg/m^3 while the average air blank corresponded to 1.5 ± 1.2 μg/m^3 (based upon a 30-L air sample). The breath samples were not corrected for this large blank because many of them were well below the blank values. The source of this discrepancy is not obvious. The tests are necessarily performed under less than ideal circumstances in a mobile unit. The opportunities for contamination are always present and the blanks only partially mimic the test conditions. Neither the pretest nor the Houston breath blanks were this high (1.2 μg/m^3 for the pretest and 0.3 to 3.5 μg/m^3 for the Harris County study).

Table 30. QUALITY CONTROL DATA FOR ST. LOUIS STUDY

Media	Date analyzed	Sample	Benzene (ng)	% Recovery
Air	10/31/79	Field Blank 1	34	
	11/1/79	Field Control 1	885	85
	11/12/79	Field Blank 1'	13	
	11/12/79	Field Control 1'	614	60
	11/14/79	Field Blank 2	89	
	11/14/79	Field Control 2	1070	98
Breath	10/27/79	Field Blank	110	
	11/2/79	Field Blank	290[a]	
	11/7/79	Field Control	1088	82
	11/8/79	Field Blank	269[a]	
	11/16/79	Laboratory Blank	152	
	11/16/79	Laboratory Control	778	63[b]
	11/21/79	Field Blank	216	
	11/21/79	Field Control	924	71[b]
	11/21/79	Field Blank	280[a]	
	11/21/79	Laboratory Blank	114	
Blood	10/11/79	Field Blank	<0.2[c]	
	10/11/79	Field Control	4.9[c]	98
Water	10/26/79	Field Blank	<0.1[c]	
	11/26/79	Field Control	39[c]	390

[a] Quantitation questionable due to interference peak in chromatogram.

[b] Breakthrough volume for benzene exceeded.

[c] Concentration in μg/L.

SECTION 9

DATA ANALYSIS

The following data were available for analysis of benzene levels in both of the sites investigated (Houston and St. Louis):

1. Overnight air samples of benzene levels collected by personal samplers that were placed in the respondent's homes,
2. Breath samples (5-20 minutes) for respondents,
3. Blood samples (only collected in the "high exposure" sampling strata),
4. Tapwater samples,
5. Limited meteorological data (wind direction, wind speed, temperature),
6. Individual answers to questions on a sample household questionnaire (e.g., demographic characteristics, where spent time, years in area, etc.), and
7. Individual sampling weights (the computation of these weights is described in Section 6).

A data file was constructed that contained the above information for each individual along with sampling strata identification (i.e., exposure = high, medium, and low).

SUMMARY STATISTICS

Table 31 presents unweighted summary statistics for air, breath, water, and blood benzene levels for the two sites (i.e., arithmetic means, medians, minimums, 90th percentiles, and maximum). Also, the percent of samples above minimal detectable is presented.

Table 31 indicates that water and blood benzene levels in the samples in Houston and St. Louis are almost always below minimum detectable (all blood samples were below minimum detectable and only 13 water samples in Houston were above minimum detectable). Thus, for the remainder of this section, analysis was performed only on air and breath benzene levels. For the two sites studied, St. Louis had higher levels of benzene in both air

Table 31. UNWEIGHTED SUMMARY STATISTICS FOR BENZENE LEVELS IN AIR, BREATH, WATER, AND BLOOD SAMPLES: BY SITE

Type of sample	Sample size[a]	% Detected[c]	Arith. mean[b]	Median	Minimum	90%[d]	Maximum
Houston							
Air	49	100.0	14.55	11.5	2.0	30.1	45.1
Breath	43	93.0	3.07	2.1	0	6.9	14.0
Water	49	26.5	0.30	0	0	1	3.0
Blood	14	0	0	0	0	0	0
St. Louis							
Air	53	100.0	24.0	17	3.4	50.2	125.0
Breath	55	100.0	7.05	5.6	1.1	13	26.0
Water	66	0	0	0	0	0	0
Blood	17	0	0	0	0	0	0

[a] Sample size = number of individuals sampled.

[b] Units: air, breath = μg/m^3; blood, water = μg/L.

[c] Percent of samples above minimal detectable limit
Min. detectable: Air [Houston] = 0.5 μg/m^3
Air [St. Louis] = 1 μg/m^3
Breath = see Section 8
Water [Houston] = 1 μg/L
Water [St. Louis] = 0.1 μg/L
Blood [Houston] = 20 μg/L
Blood [St. Louis] = 0.2 μg/L

[d] 90% = 90% of observations were less than or equal to this value.

and breath samples (e.g., Houston arithmetic means = 14.6 $\mu g/m^3$ for air and 3.1 $\mu g/m^3$ for breath versus St. Louis means of 24.0 for air and 7.1 for breath). In almost all samples taken in both sites, air and breath levels were above minimum detectable levels.

In general, the benzene levels observed in the Houston and St. Louis air samples are very low compared to published data relating health effects to benzene inhalation. For example, the observed air levels are three orders of magnitude lower than the benzene odor threshhold and three to five orders of magnitude lower than the occupational levels associated with leukemia. In fact, the current proposed NIOSH-recommended standard for occupational exposure in air is 3.13 mg/m^3 = 1 ppm. Probable health effects benzene data are discussed further in Section 10 of this report.

In addition, the air and breath levels observed were lower than those observed in RTI's pilot study in Durham of filling station attendents (on the job attendants had air levels >150 $\mu g/m^3$ and breath levels ranging from 7.2 to 27 $\mu g/m^3$, see Section 5). On the other hand, the levels in the current study were somewhat higher than those observed in the Durham pilot study and the RTI Love Canal study for nonsmoking individuals where occupational exposure was not contributory to benzene body-burden (these individuals had a mean breath level of 1.33 $\mu g/m^3$ with a range of 0.69 to 3.7 (see Section 5). Note also that individuals who smoked in the RTI Durham pilot study and the Love Canal study who were not occupationally exposed had a mean breath level of 8.42 $\mu g/m^3$ (range 1.8 to 19 $\mu g/m^3$). These breath levels are similar to the levels observed in St. Louis (recall the individuals in the current study were nonsmokers and not occupationally exposed). This discussion is summarized in Table 32.

A list of the air and breath levels along with sampling weights and exposure strata for Houston and St. Louis are given in Appendix E, Table E-1. The sampling weights are described in Section 6. Using these data, Table 33 gives weighted summary statistics for air and breath levels in the two sites. In general, the weighted means and geometric means are similar to the unweighted means and medians given in Table 31. Recall that the weighted means give an estimate of the average level of benzene for the entire area under study (i.e., (1) Harris County, Texas and (2) St. Louis City, St. Louis County, and parts of Wood River, Roxana, South Roxana and Hartford, Illinois).

DISTRIBUTION OF AIR AND BREATH LEVELS

Figure 10 gives histograms of the air and breath benzene levels in Houston and St. Louis. In general, the distributions are skewed indicating that perhaps the data are better represented by a lognormal or exponential distribution rather than the normal distribution. This would indicate that, when making statistical tests of hypotheses on benzene levels, logs of the data should be taken before tests are performed. Also, sample medians or geometric means are probably a better measure of central tendency than simple arithmetic means.

Table 32. SUMMARY OF RELATIVE BENZENE LEVELS

	Air levels ($\mu g/m^3$)	Breath levels ($\mu g/m^3$)
Probable Health Effects		
Leukemia	$3\text{-}15 \times 10^5$	
Odor	3×10^5	
RTI Pilot Study (Durham)		
On-the-job filling station attendents	>150	7.2 - 27
RTI Pilot Study (Durham and Love Canal)		
Nonsmoking, nonoccupational exposure (NOE)		.69 - 3.7
RTI Pilot Study (Durham and Love Canal)		
Smokers (S), nonoccupational exposure (NOE)		1.8 - 19
Current Study (NS, NOE)		
Houston	2 - 45	0 - 14
St. Louis	3 - 125	1 - 26

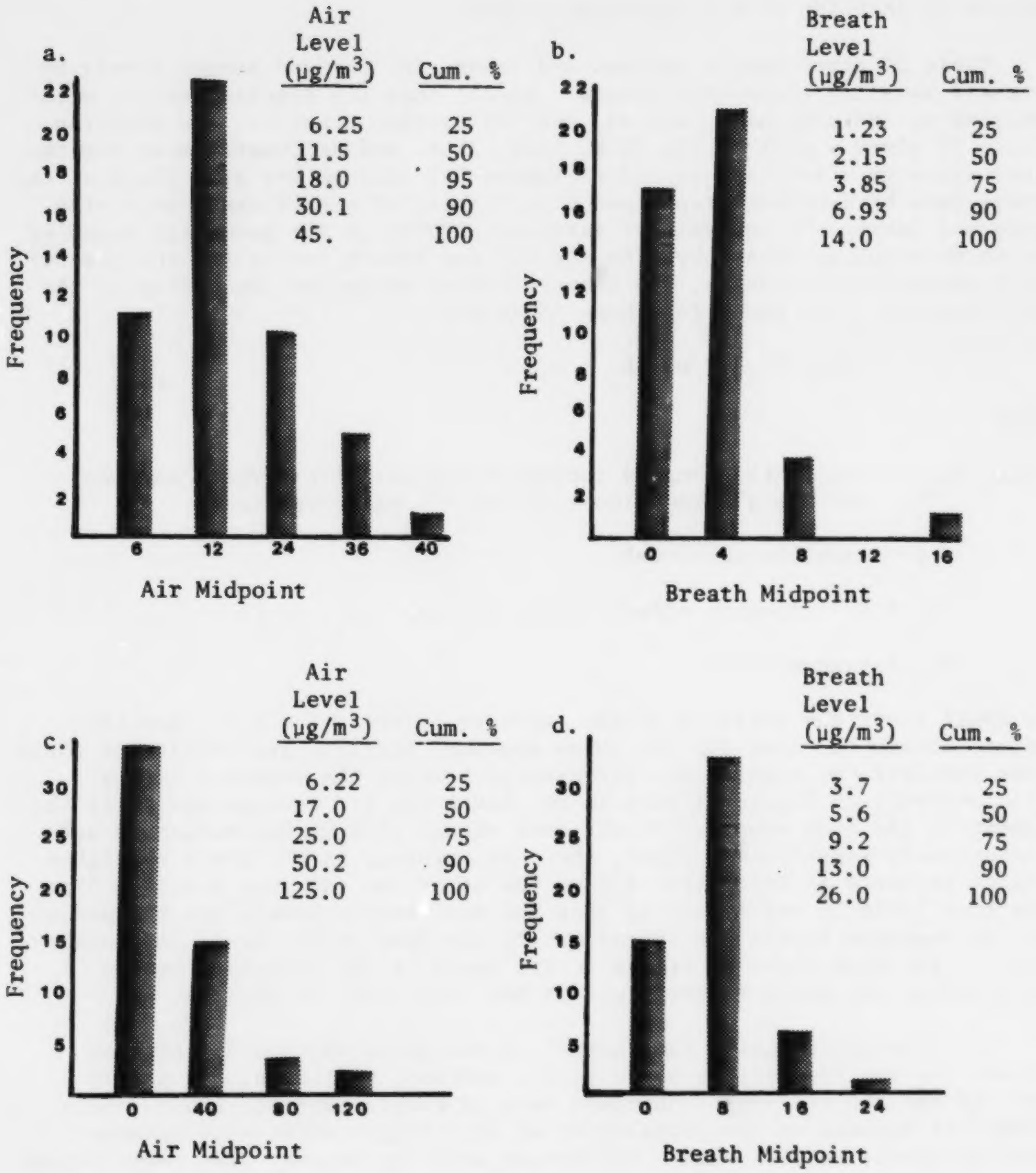
Table 33. WEIGHTED MEANS AND STANDARD ERRORS FOR AIR AND BREATH BENZENE LEVELS: BY SITE

	Sample size[a]	Weighted mean[b] (μg/m^3)	Standard error of mean[c]	Weighted geometric mean[c] (μg/m^3)
Houston				
Air	49	16.1	1.84	12.4
Breath	43	2.93	.48	2.51
St. Louis				
Air	53	26.8	8.1	15.0
Breath	55	8.5	1.5	6.81

[a] Sample size = number of individuals sampled.

[b] Weighted means are an estimate of the benzene level for air and breath in the area sampled (see sampling section).

[c] Standard error is an estimate of the standard error of the weighted mean.



a.

Air Level ($\mu g/m^3$)	Cum. %
6.25	25
11.5	50
18.0	95
30.1	90
45.	100

b.

Breath Level ($\mu g/m^3$)	Cum. %
1.23	25
2.15	50
3.85	75
6.93	90
14.0	100

c.

Air Level ($\mu g/m^3$)	Cum. %
6.22	25
17.0	50
25.0	75
50.2	90
125.0	100

d.

Breath Level ($\mu g/m^3$)	Cum. %
3.7	25
5.6	50
9.2	75
13.0	90
26.0	100

Figure 10. Frequency bar charts for benzene. a. air levels in Houston, TX; b. breath levels in Houston, TX; c. air levels in St. Louis, MO, and d. breath levels in St. Louis, MO.

MEDIANS BY SAMPLING STRATA (EXPOSURE STRATA)

Table 34 gives sample medians and ranges for air and breath levels by site and sampling (exposure) strata. Recall that the sampling strata were designed to indicate high, medium, and low benzene exposure. In addition, Figure 11 gives a plot of the 25th, 50th, 75th, and arithmetic mean for the three exposure strata and Appendix Figures E-1 through E-4 give plots of the actual data by exposure strata and site. Tests of significance were also performed (using the analysis of variance, ANOVA) on the geometric means of the three sampling strata by site for air and breath levels (in the case of the lognormal distribution, the geometric mean estimates the median of the distribution). The model for these ANOVA was:

$$\log_e(B)_{ij} = \mu + L_i + \varepsilon_{ij} \qquad (1)$$

where

$\log_e(B)_{ij}$ = log of the benzene concentration in air or breath samples for the j^{th} individual in the i^{th} exposure strata,

μ = mean benzene level,

L_i = i^{th} exposure effect (high, medium, low),

ε_{ij} = random error.

The ANOVA tests the equality of the exposure effects, L_i, i.e., are the benzene levels the same for the three exposure strata. The results of these tests indicated no significant differences between the exposure strata. Note, however, in Figure 11 that in St. Louis the air benzene median is the highest in the high exposure strata even though this higher median is not statistically significant. Thus, there is evidence in St. Louis of higher benzene exposure at Wood River versus the other two exposure strata. Also note from Table 34 and Figure 11 that the air benzene levels for the medium and low exposure strata are approximately the same in St. Louis and Houston. That is, the high exposure strata in St. Louis is the principal reason St. Louis median air benzene levels are higher than those in Houston.

RTI also investigated the "power" of detecting various differences between the sampling strata based on the medians, variances, and sample sizes of the air and breath observed data in Houston and St. Louis. Here "power" is defined as the probability of detecting a difference between sampling strata medians when a difference actually exists. The computations were based on detecting a difference between the low versus the high sampling strata medians. The results are found in Table 35.

In addition to the above, the correlations between exposure strata and air and breath levels were computed and are given in Table 36. Table 36 shows that the correlations are relatively small, and Appendix Figures E-1 through E-4 indicate why this is so. For example, in St. Louis for air, Figure E-3 shows that two relatively high air values in the medium and low exposure strata (125 and 118 $\mu g/m^3$, respectively) result in a -0.02 correlation

Table 34. UNWEIGHTED SAMPLE MEDIANS AND RANGES FOR AIR vs. BREATH LEVELS BY SITE AND SAMPLING STRATA

City	Sampling strata		Air ($\mu g/m^3$)	Breath ($\mu g/m^3$)	Approx. sample size
Houston TX	Low	Median	13.0	1.7	16
		Range	(3.4-27)	(0-8.2)	
	Median	Median	11.0	2	18
		Range	(2-45)	(1-4.8)	
	High	Median	12.0	3.1	15
		Range	(3.1-35)[a]	(0-14)[a]	
St. Louis MO	Low	Median	10.0	5.4	18
		Range	(3.4-118)	(1.1-18)	
	Median	Median	13.0	7.0	12
		Range	(3.5-125)	(2.3-26)	
	High	Median	17.0	4.7	23
		Range	(3.7-86)[a]	(1.6-16)[a]	

[a] Tests of significance did not indicate significant differences between estimated medians across sampling strata.

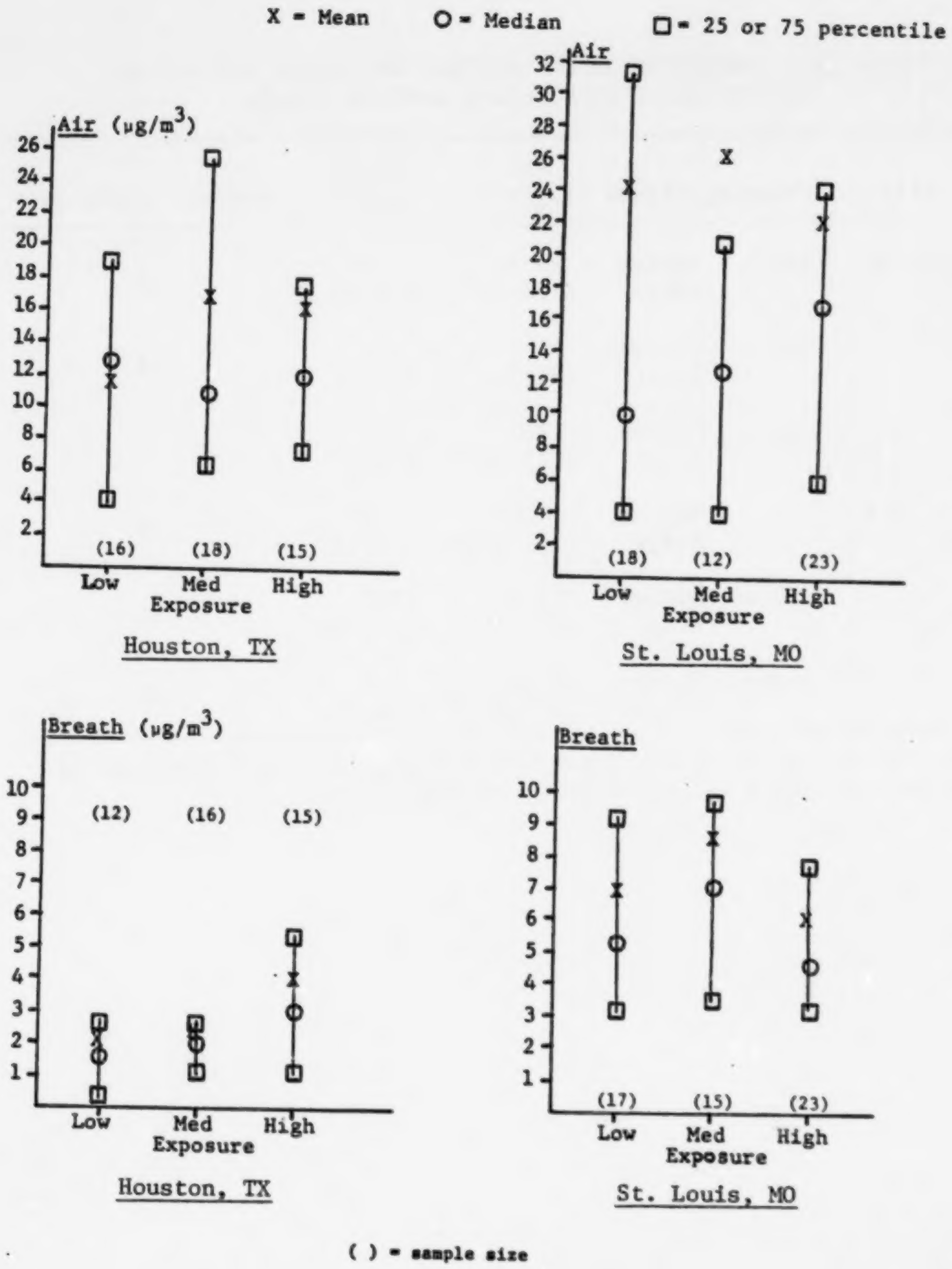


Figure 11. Percentile plots of benzene levels in air and breath; by site and exposure strata.

Table 35. POWER OF DETECTING VARIOUS DIFFERENCES BETWEEN THE HIGH AND LOW SAMPLING STRATA[a]

Difference between medians (%)	Houston		St. Louis	
	Air	Breath	Air	Breath
50[b]	.52	.40	.33	.63
100	.89	.77	.64	.96
200		.98	.94	

[a] Computations based on a one-tailed test at the 0.05 level of significance.

[b] 50 = High strata median is 50 percent higher than the low strata median.

Table 36. CORRELATIONS BETWEEN AIR AND BREATH LEVELS VS. EXPOSURE STRATA: BY SITE

	Houston, TX		St. Louis, MO	
	Air	Breath	Air	Breath
Spearman	+ .06	+ .23	- .02	.09
Unweighted Pearson	+ .08	+ .23	.03	.11

between air and exposure strata. Thus, the overall low benzene levels observed in the study, coupled with limited sample sizes and a few outlying values, result in levels in the various exposure strata that are not significantly different.

CORRELATIONS BETWEEN AIR AND BREATH BENZENE LEVELS

Several correlations between air and breath benzene levels were also computed. The results are given in Table 37 (recall air levels were by personal monitor in the participant's home). In addition, Figures 12 through 14 present plots of breath by air benzene levels by site. The scales of all figures are the same and this is why the Houston plot is clustered in the left corner (recall Houston had lower benzene levels than did St. Louis). The table and figures show that there is no apparent relationship between the relatively low air and breath benzene levels in Houston. On the other hand, in St. Louis there is some evidence of a positive relationship (unweighted Pearson correlation = 0.49). However, care must be taken not to overinterpret this result since the apparent relationship is based on only a few high air and breath values; the majority of the values being clustered in the left corner of the plots. The reason the weighted Pearson correlation (=0.73) is higher than the unweighted correlation can be seen in Figure 13, which shows the relative weight given each data point. The figure shows that the largest data point (air = 125 and breath = 26 $\mu g/m^3$) receives a relatively large sampling weight resulting in a moderately high-weighted Pearson correlation.

To further examine the relationship between the two media, the mean breath levels were computed for air categories above and below 20 $\mu g/m^3$, by site. These results are given in Table 38, which again indicates that in St. Louis there is some relationship between air and breath levels. However, a test of the breath means in St. Louis (6.33 vs. 8.76 $\mu g/m^3$) for the two air categories was not significant at the 0.10 level.

EXPOSURE BASED ON WIND DIRECTION

Using meteorological data based on the prevailing wind, air and breath benzene levels upwind and downwind of benzene sources in Houston and St. Louis were examined. The Houston results are given in Table 39. Note that historical prevailing wind was used to define upwind and downwind in Houston since benzene sources were quite spread out and it was not considered feasible to use daily prevailing wind. In addition, three segments that were downwind but outside the Houston city limits were not included in the downwind strata (see Figure 4). Table 39 shows that there is evidence of higher levels for air and breath in the downwind strata (e.g., air medians of 11 versus 14 $\mu g/m^3$). However, tests of significance for these medians were not significant at the 0.10 level (the model used for testing is the same as that given in equation [1]).

Table 40 gives upwind and downwind benzene levels for the Wood River area (the high exposure strata in St. Louis). In this case, the prevailing wind on the day the measurements were taken was used to define upwind and downwind strata. Again, there is evidence that the downwind strata have

Table 37. PEARSON AND SPEARMAN CORRELATIONS BETWEEN AIR AND BREATH BENZENE LEVELS: BY SITE

	Pearson[a]		Spearman	
	Houston	St. Louis	Houston	St. Louis
Unweighted	-.08	.49[b]	-.07	.15
Weighted	-.11	.73[b]	X	X
Unweighted log	-.14	.24	X	X
Weighted log	-.09	.24	X	X

[a] Pearson correlations assume the data are normally distributed while Spearman correlations are based on ranks and do not assume normally.

[b] Significant from zero at 0.01 level.

X = Since Spearman correlations are based on ranks, they are not computed for weighted or logged data.

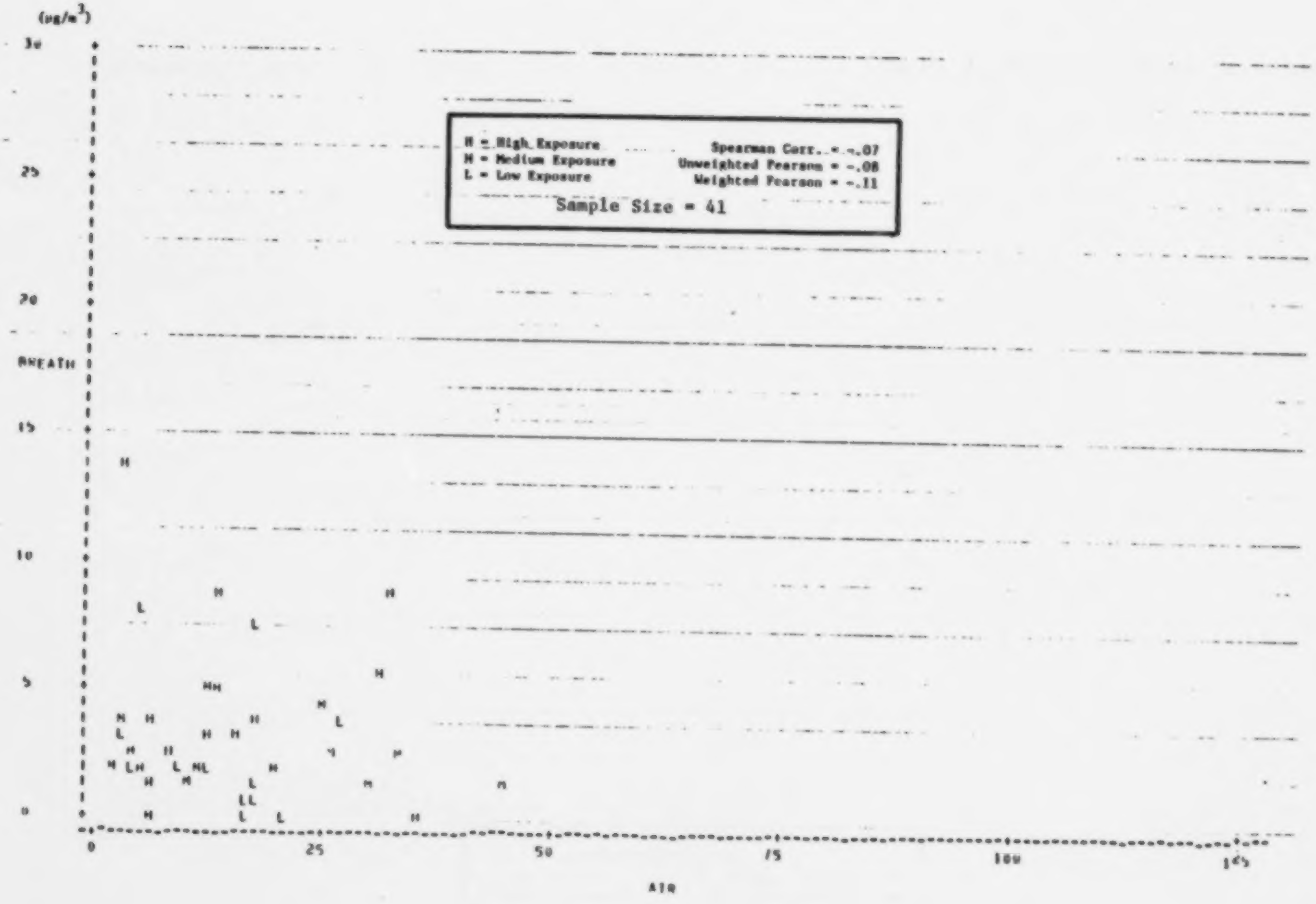


Figure 12. Site = Houston. Plot of breath vs. air; symbol is value of exposure stratum.

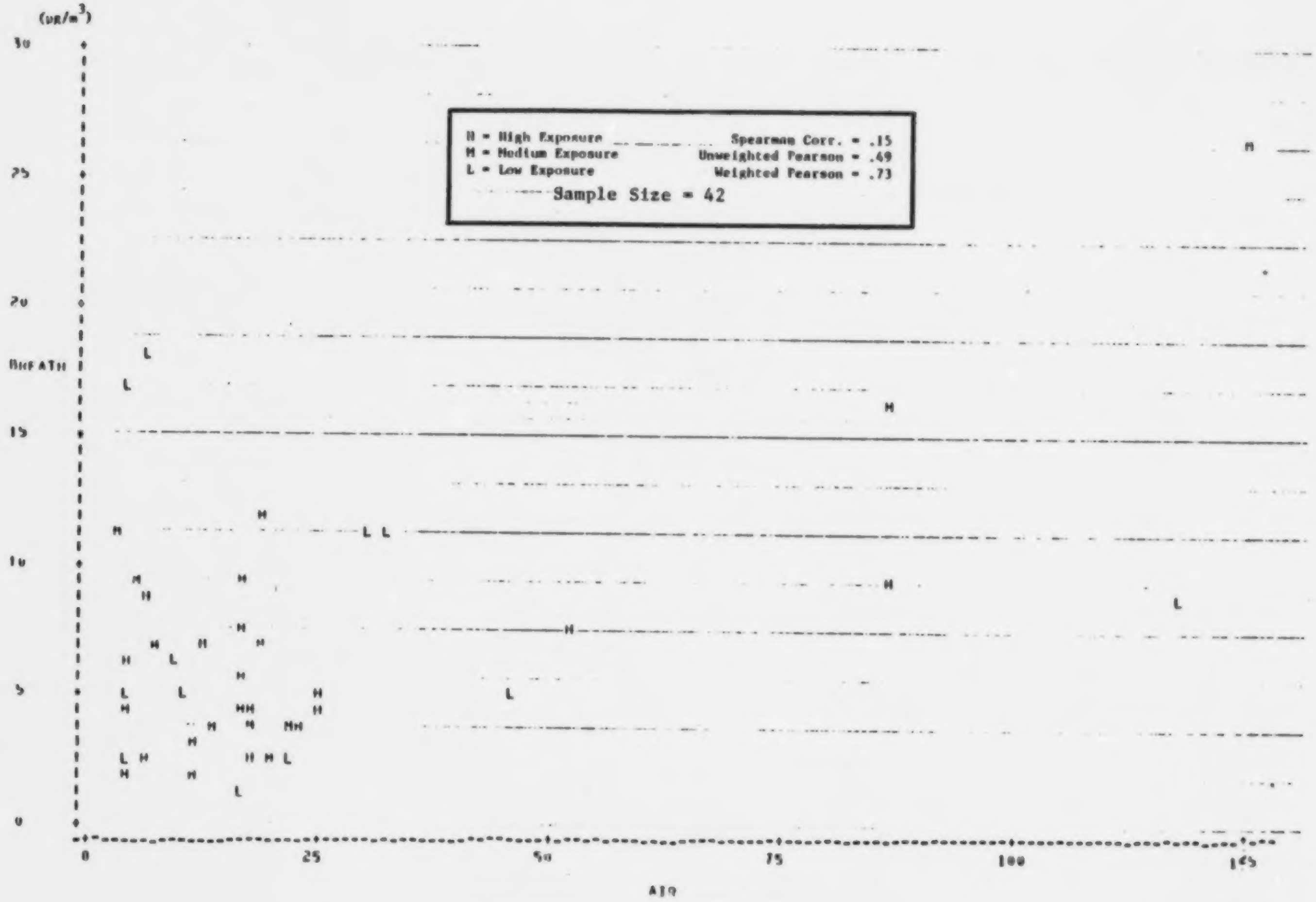


Figure 13. Site = St. Louis. Plot of breath vs. air; symbol is value of exposure stratum.

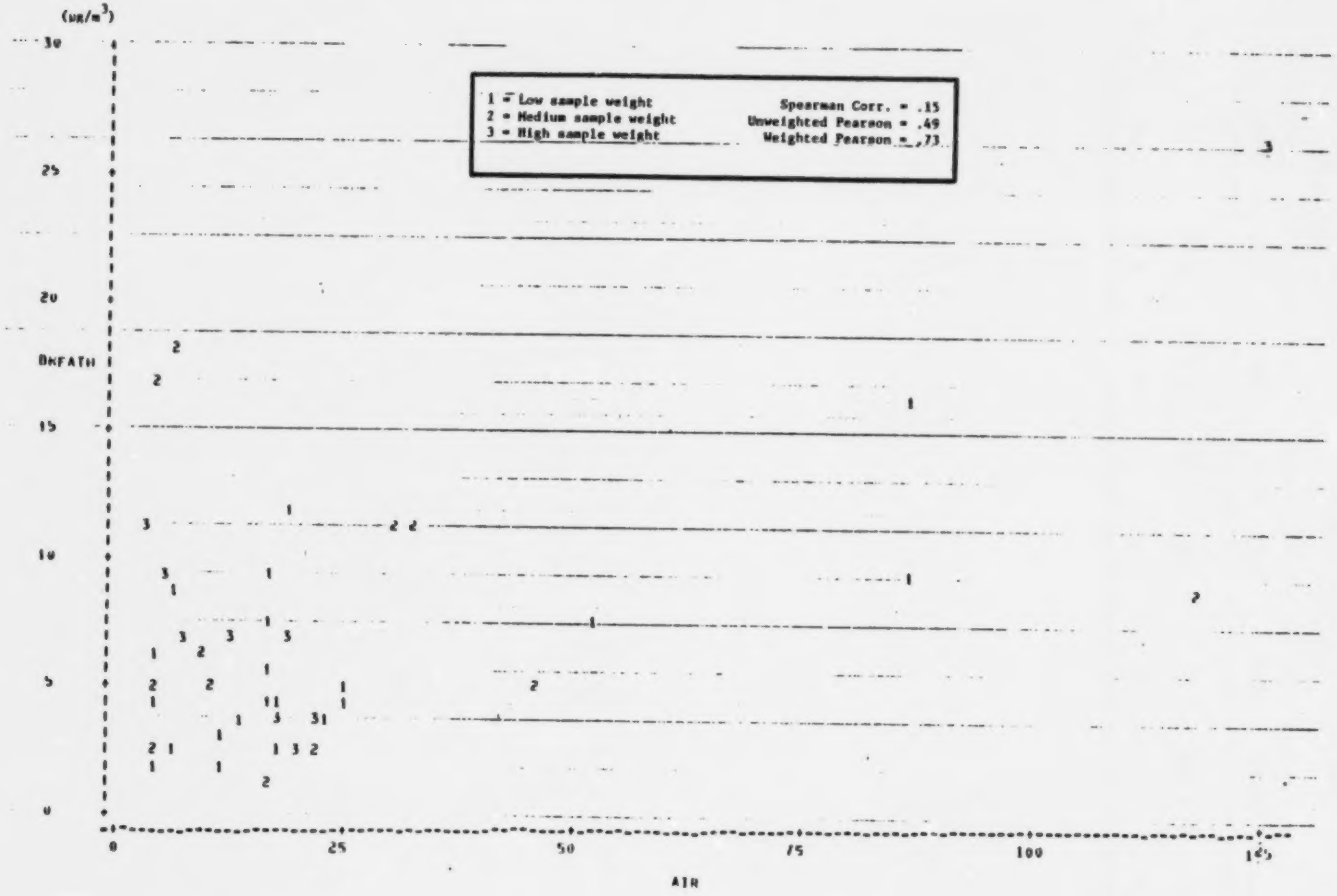


Figure 14. Site = St. Louis. Plot of breath vs. air; symbol is categorized value of weights.

Table 38. SUMMARY STATISTICS FOR BENZENE LEVELS IN BREATH FOR TWO CATEGORIES OF AIR LEVELS: BY SITE

	Houston, TX, air levels (μg/m^3)				St. Louis, MO, air levels (μg/m^3)			
Air levels	Mean	Min.	Max.	n	Mean	Min.	Max.	n
<20 μg/m^3	3.18	0	14	30	6.33	1.1	18	29
>20 μg/m^3	3.11	0	9	11	8.76	2.2	26	13

Table 39. SAMPLE MEDIANS FOR AIR AND BREATH LEVELS UPWIND AND DOWNWIND OF BENZENE SOURCES IN HOUSTON[a]

		Upwind	Downwind	
Air	Median	11[b]	14	(NS)[c]
	Range	2-33	3.1-45	
	n	25	24	
Breath	Median	2	3.1	(NS)
	Range	0-8.2	0-14	
	n	22	21	

[a] Upwind and downwind by historical prevailing wind (not prevailing wind on day measurements were taken). That is, downwind defined by segments <20, 22, 23, 29 and 33. See data listing in Appendix E and Figure 4.

[b] Units: μg/m^3.

[c] NS = Not significant at the 0.10 level.

Table 40. SAMPLE MEDIANS FOR AIR AND BREATH LEVELS UPWIND AND DOWNWIND OF BENZENE SOURCES IN WOOD RIVER (THE HIGH EXPOSURE STRATA OF ST. LOUIS)[a]

		Upwind	Downwind	
Air	Median	14	17	(NS)[b]
	Range	6.2-23	3.7-86	
	n	6	17	
Breath	Median	3.8	5.5	(NS)
	Range	2.5-8.9	1.6-16	
	n	5	18	

[a] Upwind and downwind defined by prevailing wind on day the measurements were taken.

[b] NS = Not significant at the 0.10 level.

higher air and breath levels but tests of significance were not significant at the 0.10 level. Thus, in both Houston and St. Louis there is some evidence that higher air and breath levels are present downwind from the benzene sources.

QUESTIONNAIRE VARIABLES

Table 41 presents frequencies of various questionnaire variables for the individuals sampled, by site. A copy of the questionnaire is given in Appendix D. The table shows that over 60 percent of respondents were white, almost all respondents considered themselves to be in good health, over 90 percent used air conditioning or an evaporative cooler, most used a municipal water supply for drinking, 25 percent had individuals in the household who had hobbies potentially involving benzene products (painting, furniture refinishing, scale models, or gardening) and approximately 40 percent had lived at their current address for 0-4 years.

To further investigate the possible effect of these questionnaire variables on individual benzene levels a one-way analysis of variance (ANOVA) was run on air and breath levels for each of the variables in Table 40.

The model for this analysis was:

$$B_{ij} = \mu + Q_i + \varepsilon_{ij} \qquad (2)$$

where

B_{ij} = benzene level in air and breath for the j^{th} individual in the i^{th} questionnaire variable category (e.g., age, health status, etc.)

μ = mean benzene level

Q_i = effect of the i^{th} questionnaire variable category,

ε_{ij} = random error.

The ANOVA tested the equality of the Q_i's; i.e., are the benzene levels the same for the various variable categories. The results of the ANOVAs are also given in Table 41 along with sample means by variable categories. The table shows that in general very few of the sample means were significantly different. This is undoubtedly due to relatively low benzene levels in the two sites and the limited sample sizes. The only significant results found were the following:

1. In Houston

   a. Air levels for "years lived in this area," "grow own food," and "household smoke";,

Table 41. FREQUENCIES FOR QUESTIONNAIRE VARIABLES: BY SITE

Variable	Categories	Code	Houston		Results of tests of significance[a] (units = $\mu g/m^3$)		St. Louis		Results of tests of significance[a] (units = $\mu g/m^3$)	
			N[b]	%	Air means	Breath means	N	%	Air means	Breath means
1. Sex	Male	1	21	42.0	14.4	3.0	24	35.3	24.0	6.2
	Female	2	29	58.0	14.7	3.2	44	64.7	24.0	7.5
2. Race	White	1	30	60.0	12.8	2.7	45	66.1	25.8	7.4
	Black	2	6	12.0	13.2	2.7	9	13.23	8.4	5.7
	Asian		0	-			2	2.9		
	Hispanic	3	13	26.0	18.7	4.0	0	-	25.1	6.9
	Am. Indian/Alaska		1	2.0			1	1.4		
	Other		0	-			11	16.1		
3. Avg. hours outside each day	0-2	1	14	28.0	13.4	3.5	38	55.9	29.4	7.2
	3-5	2	25	50.0	15.8	2.9	19	27.9	18.3	8.0
	≥6	3	11	22.0	13.3	3.0	11	16.1	14.2	4.8
4. Hours away from home on weekday	0-7	1	22	44.0	15.3	3.1	21	30.9	30.4	7.6
	≥8	2	28	56.0	14.0	3.1	47	69.1	21.5	6.8
5. Hours away from home on weekend	0-4	1	26	51.0	14.6	2.5	25	36.8	22.7	6.2
	≥5	2	24	49.0	13.8	3.5	35	63.2	24.9	7.6
6. Current health status	Excellent	1	26	52.0	12.4	3.3	41	60.3	21.0	7.9
	Good	2	21	42.0	16.8	2.9	27	39.7	28.6	6.0
	Fair		3	6.0			0	-		
7. Ever treated for anemia	Yes	1	12	24.0	13.9	4.6 (0.9)	8	11.8	28.4	5.2
	No	2	38	76.0	14.8	2.7	60	88.2	23.4	7.3
8. Years lived in this area	0-4	1	23	46.0	13.9	2.6	11	14.9	36.2	7.7
	5-15	2	11	22.0	9.8 (.09)	3.9	24	35.8	28.4	8.7
	≥16	3	16	32.0	18.4	3.1	33	49.3	18.4	5.8
9. Way cool home	Air cond. or evap. cooler	1	49	98.0	14.2*	2.9	63	92.6	24.6	7.1
	fan only	2	1	2.0	32.0	9.0	5	7.4	8.5	5.8

(continued)

Table 41 (continued)

Variable	Categories	Code	Houston N^b	Houston %	Results of tests of significance[a] (units = μg/m³) Air means	Results of tests of significance[a] (units = μg/m³) Breath means	St. Louis N	St. Louis %	Results of tests of significance[a] (units = μg/m³) Air means	Results of tests of significance[a] (units = μg/m³) Breath means
10. Grow own Food in home garden	Yes	1	8	16.0	8.5(.08)	4.5	24	36.4	31.9	9.1 (.03)
	No	2	42	84.0	15.6	2.8	42	63.6	19.9	6.0
11. Source of drinking water	Tap municipal Supply	1	37	74.0	15.2	3.4	66	97.1	24.1 *	7.1 *
	Other	2	13	26.0	12.8	2.3	2	2.9	17.0	5.2
12. Does anyone use in household smoke	Yes	1	10	20.0	20.0 (.05)	4.8 (.04)	24	35.3	18.1	5.2 (.04)
	No	2	40	80.0	13.1	2.6	44	64.7	27.3	8.1
13. Anyone have job with benzene prod.	Yes	1	5	10.0	11.8	1.9	8	11.8	21.8	6.8
	No	2	45	90.0	14.8	3.2	60	88.2	24.4	7.1
14. Anyone have hobby using benzene prod.	Yes	1	12	24.0	12.4	4.7 (.04)	17	25.0	23.4	5.0 (.09)
	No	2	38	76.0	15.2	2.6	51	75.0	24.2	7.7
15. Others in house treated for anemia	Yes	1	5	10.0	14.7	3.8	4	5.9	5.1	4.0
	No	2	43	86.0	14.5	3.0	64	94.1	25.1	7.3
	Do not know		2	4.0			0	-		
16. Age	20-30	2	19	38	15.8	2.8	13	19.1	20.2	7.2
	31-40	3	23	46.0	13.6	4.0	29	42.5	26.5	7.9
	≥41	4	8	16.0	14.6	1.5	26	38.3	22.2	6.0
17. Weight	100-125	2	15	30.0	15.6	3.6	11	14.7	31.2	7.0
	126-150	3	9	18.0	9.3	2.2	22	32.7	23.1	7.8
	151-175	4	12	24.0	12.4	2.6	17	25.1	17.9	7.0
	176-200	5	13	26.0	19.3	3.6	10	14.7	13.9	6.7
	≥201	6	1	2.0	11.0	2.0	8	11.8	32.7	5.9

(continued)

Table 41 (continued)

Variable	Categories	Code	Houston		Results of tests of significance[a] (units = $\mu g/m^3$)		St. Louis		Results of tests of significance[a] (units = $\mu g/m^3$)	
			N[b]	%	Air means	Breath means	N	%	Air means	Breath means
18. Height	≤60	1	3	6.0	19.0	6.5	1	1.5	52.0	7.7
	61-66	2	24	48.0	14.9	2.5	36	53.1	23.9	7.4
	67-72	3	18	36.0	14.2	2.8	28	41.3	24.6	7.0
	≥72	4	5	10.0	11.2	4.1	3	4.4	11.8	3.3
19. Numbers eggs eaten past 48 hours	0	0	20	40.8	14.5	2.8	35	51.5	31.1	6.9
	1	1	10	20.4	11.5	3.2	10	14.7	14.4	6.4
	2	2	14	28.6	14.3	2.4	14	20.6	18.3	7.0
	≥3	3	5	10.2	15.0	5.7	9	13.3	13.1	8.6
20. Yrs lived at this address	0-4	1	29	58.0	14.8	2.6	26	38.8	24.4	7.2
	5-15	2	16	32.0	13.8	4.0	28	41.9	25.7	7.4
	≥16	3	5	10.0	15.6	2.5	13	19.6	21.9	6.6

---

[a] N = Number of individuals (Note: Due to the fact that not all individuals had air and breath levels, the air and breath means are based on fewer observations than N).

[b] The tests of significance tested if the benzene air and breath mean levels were the same for the various questionnaire variable categories. (0.05) = significant at the 0.05 level of significance. Blank = not significant at the 0.10 level of significance.

[*] Not tested because of limited sample size in at least one category.

b. Breath levels for "treated for anemia," "household smoke," and "hobby".

2. In St. Louis

a. Breath levels for "grow own food," "household smoke," and "hobby."

ANOVAs were also run using model (2) with the $\log_e$ of benzene air and breath levels as the dependent variable. The results were quite similar to those given in Table 41.

In addition to the ANOVAs, stepwise regressions were also run on the air and breath levels by site (these regressions were also run on the logs of air and breath levels). The general model for this analysis was

$$B_j = \mu + B_1 \text{ (Ques. Var.}_{1j}) + B_2 \text{ (Ques. Var.}_{2j}) + \ldots, + e_j \qquad (3)$$

where

$B_1, B_2 \ldots$ = regression parameters,

B_j = the benzene level in air or breath for the jth individual

e_j = random error

The purpose of the stepwise regressions was to indicate which questionnaire variables appeared to be the most important in predicting benzene levels.

In brief, the stepwise regression procedure used consists of the following approach. The stepwise computer program finds the single-variable model (i.e., air benzene level on only one variable) which produces the largest R^2 statistics (where R^2 is the square of the multiple correlation coefficient). After entering the variable with the largest R^2, the program uses the partial correlation coefficients to select the next variable to enter the regression. That is, the program enters the variable with the highest partial correlation coefficient with air benzene level (given that the variables with the largest R^2 are already in the model). An F test is performed to determine if the variable to be entered has a probability greater than the specified "significance level for entry." After a variable is added, the program looks at all the variables already included in the model and computes a partial F-statistic to determine if these variables should remain in the model. Any variable not producing a partial F significant at the specified "significance level for inclusion" is then deleted from the model. The process then continues by determining if any other variables should be added to the regression. The process terminates when no variable meets the conditions for inclusion or when the next variable to be added to the model is one just previously deleted from it. For the present analysis, all variables in the final regression model were deemed significant at the 0.10 level of significance.

The results of running the stepwise regression by site are given in Table 42 for both air and breath benzene levels and the log of air and breath benzene levels. The log results are similar to the original unit results. In general, the table shows that the correlations for the regressions are relatively small (<0.60 for all cases). In addition, the results are difficult to interpret considering that the sign on the regression coefficients is quite often in the opposite direction from that expected. For example, for breath in St. Louis, "does anyone else in household smoke" has a positive regression coefficient (i.e., lower breath levels in households with smokers, see Table 41) and "anyone have hobby using benzene products" also has a positive regression coefficient (i.e., low breath levels in households with benzene hobbies). Therefore, in general, the stepwise regressions do not indicate that the questionnaire variables explain the variation in the air and breath levels. Again, this is undoubtedly due to low benzene levels and limited sample sizes.

Finally, Table 43 gives answers to the questionnaire variables for four selected individuals with relatively high air or breath levels (two individuals in Houston and two in St. Louis). The individuals' air and breath benzene levels are given in the table and Appendix Figures E-1 through E-4 indicate why these four individuals were selected. It is not obvious from Table 43 why these four individuals had high air or breath benzene levels.

Table 42. RESULTS OF STEPWISE REGRESSIONS[a] BY SITE WITH AIR AND BREATH BENZENE LEVELS AS THE DEPENDENT VARIABLE (ALSO LOG [AIR] AND LOG [BREATH] BENZENE LEVELS)

	Air[b]	Log (air)	Breath	Log (breath)
Houston				
	[+] Years in Area (8) [-] Other Smoke (12) [-] Years at Address (20)	[+] Years in Area (8) [+] Grow Food (10)	[-] Other Hobby (14) [-] Other Smoke (12) [+] Race (2)	[-] Other Hobby (14) [+] Race (2)
N	47	47	41	41
R^2=(corr)^2	.27	.19	.33	.25
R=corr.	.52	.44	.57	.50
St. Louis				
	[-] Eggs (19)	[-] Eggs (19)	[-] Grow Food (10) [+] Other Hobby (14) [+] Other Smoke (12) [-] Other Job (13) [-] Weight (17)	[-] Grow Food (10) [+] Other Hobby (14) [+] Other Smoke (12) [+] Sex (1)
N	50	50	53	53
R^2=(corr)^2	.08	.09	.34	.35
R=corr.	.28	.30	.58	.59

[a] Stepwise procedure set up so that all variables in final equation are significant at 0.10 level.

[b] Air column indicates that Air Benzene level = linear function (years in area, other smoke, years at address). The correlation coefficient for this regression is 0.52.

[ ] sign on regression coefficient (e.g., [+] = years lived in this area has a positive regression coefficient).

( ) question number in Table 39 (e.g., [8] = years lived in this area).

Table 43. ANSWERS TO QUESTIONNAIRE FOR SELECTED INDIVIDUALS WITH HIGH AIR OR BREATH BENZENE LEVELS

Variable	Categories	Houston		St. Louis	
		Indiv. 1 air = 3.1 $\mu g/m^3$ Breath = 14	Indiv. 2 = 45 = 1	Indiv. 1 Air = 125 Breath = 26	Indiv. 2 = 118 = 8.8
1. Race	Male Female	Male	Male	Female	Male
2. Race	White Black Asian Hispanic Am. Indian/Alaska Other	White	Other	White	White
3. Avg. Hrs. Outside Each Day	0-2 3-5 ≥6	≥ 6	≥ 6	0-2	0-2
4. Hours Away From Home on Weekday	0-7 ≥8	≥ 8	≥ 8	0-7	≥ 8
5. Hours Away From Home on Weekend	0-4 ≥5	≥ 5	0-4	≥ 5	≥ 5
6. Current Health Status	Excellent Good Fair	Good or Fair	Good or Fair	Excellent	Good or Fair
7. Ever Treated for Anemia	Yes No	No	No	No	Yes

(continued)

Table 43 (continued)

Variable	Categories	Houston Indiv. 1 air = 3.1 $\mu g/m^3$ Breath = 14	Houston Indiv. 2 = 45 = 1	St. Louis Indiv. 1 Air = 125 Breath = 26	St. Louis Indiv. 2 = 118 = 8.8
8. Years Lived in This Area	0-4 5-15 $\geq$16	5-15	0-4	5-15	5-15
9. Way Cool Homes	Air Cond. or Evap. Cooler Fan Only	AC or Cooler	AC or Cooler	AC or Cooler	AC or Cooler
10. Grow Own Food in Home Garden	Yes No	Yes	No	No	Yes
11. Source of Drinkking Water	Tap Municipal Supply Other	Tap. Mun.	Other	Tap Mun.	Tap Mun.
12. Does Anyone Else in Household Smoke	Yes No	Yes	No	No	No
13. Anyone Have Job With Benzene Prod.	Yes No	No	No	No	No
14. Anyone Have Hobby Using Benzene Prod.	Yes No	Yes	No	No	No
15. Others in House Treated for Anemia	Yes No Do Not Know	No or don't know	No or don't know	No or don't know	No or don't know

(continued)

Table 43 (continued)

Variable	Categories	Houston Indiv. 1 air = 3.1 μg/m^3 Breath = 14	Houston Indiv. 2 = 45 = 1	St. Louis Indiv. 1 Air = 125 Breath = 26	St. Louis Indiv. 2 = 118 = 8.8
16. Age	21-30 31-40 $\geq$41	31-40	31-40	31-40	$\geq$41
17. Weight	100-125 126-150 151-175 176-200 $\geq$201	176-200	176-200	100-125	$\geq$201
18. Height	$\leq$60 61-66 67-72 $\geq$72	67-72	67-72	61-66	67-72
19. Numbers Eggs Eaten Past 48 hrs.	0 1 2 $\geq$3	$\geq$ 3	Missing	None	None
20. Yrs Lived At This Address	0-4 5-15 $\geq$16	5-15	0-4	5-15	5-15

SECTION 10

DISCUSSION OF THE HEALTH EFFECTS OF BENZENE

Benzene exposure has been implicated in the development of hematotoxicity in humans and animals (35,36,37). In humans, benzene exposure may induce chromosomal aberration, pancytopenia, and leukemia (36). However, information about the human health effects associated with benzene exposure remain incomplete, and animal studies have been important in assessing and predicting the toxicological effects of such exposure on humans. It should be noted that no animal model has yet been found for the leukemogenic effect of benzene found in humans. Furthermore, the exposures that produced leukemia in some occupationally exposed individuals were varioualy estimated between 10 and 1000 ppm (3.1×10^4 to 3.1×10^6 $\mu g/m^3$). The health effects of benzene have been reviewed recently (6). Some effects such as chromosome breakage have been noted at chronic exposures as low as 2 to 3 ppm (time-weighted average) (38). When compared to the highest air benzene levels found in the two sites, 0.04 ppm, the question of the potential health effect revolves around the representative nature of the limited air sampling in this study and the safety factors that should be applied.

The toxicology (6,7,12) and metabolism (3,12) of benzene have been reviewed recently. Benzene is efficiently (~30-50 percent) absorbed by the lungs, which represents the major route of exposure, both occupational and environmental. Percutaneous absorption appears to be an unlikely contributor to environmental exposure. While oral ingestion of benzene may be significant, it would be expected to appear equally in the control populations.

METABOLISM OF BENZENE IN ANIMALS

The metabolism of benzene in animals appears to proceed along similar pathways (39,40). Of the routes of exposure, inhalation of benzene in animals is the route that most closely approximates the primary means of human exposure (40). By this route of administration, benzene is absorbed into the respiratory system where the reagent quickly reaches equilibrium with alveolar air. A portion of the benzene is eliminated unchanged in the expired air, and the actual rate of removal is probably determined by the vapor pressure of benzene in the lung and its concentration in the blood, which in turn depends on the rate of absorption and metabolism (39,40).

Of the remainder, another small portion of benzene, due to its high lipid solubility, is partitioned and absorbed in the adipose tissues and bone marrow, where it may undergo further metabolism. The majority of the benzene is transported via blood to the liver, the principal organ of benzene metabolism (39). The rate of benzene metabolism and its tissue distribution patterns depend on the route of administration in the animal and probably reflect the circulatory sequence from the point of administration to the liver (39).

Once absorbed, benzene is rapidly distributed in the blood, where it is eliminated or metabolized. According to most reports, 30 to 50 percent of the absorbed benzene is exhaled through the lungs. The remainder is fixed in the bone marrow, fatty tissues, and liver where it is metabolized. Only 0.1 to 0.2 percent of the benzene is eliminated unchanged in the urine. About 20 to 30 percent of the absorbed benzene is oxidized to phenol and eliminated in the urine as the glycinate, sulfate, or glucuronide ester. A wide variety of minor and trace (<5 percent) metabolites have been detected in humans and laboratory animals including pyrocatechol, hydroquinone, hydroxyquinol and sundry ring-cleavage products. It has been reported (41) that up to 8 percent of the urinary phenols are excreted in the free form. Excretion in the feces (in rabbits) appears to be negligible (42) with only 0.5 percent of a radioactive dose detected. Benzene accumulation in the body apparently occurs in the fat deposits (43), although only 2.6 percent of a benzene dose was found in rabbit fat 2 days after exposure (42). Thus, the major excretion routes are exhalation of benzene and as a conjugated phenol in the urine.

Animal studies with labelled benzene indicate that the elimination of the reagent via the lung and urine accounts for the principle detoxification pathways (39). In expired air, a large percentage is eliminated as unchanged benzene. In the urine, the principal oxidative products are the alkaline salts of phenylsulfuric and phenylglucuronic acids. The predominant form of the final urine metabolites seems to be species-dependent in animals. In mice, the glucuronide form predominates while in rats, dogs, cats, and humans, the sulfate formation is preferred (39).

The kinetics of metabolism and excretion are not well-defined. Benzene is eliminated rapidly through the lungs, but apparently exhibits two rate constants; one which applies over the first 60 min after exposure and one which applies over longer periods (8). The biological half-life of benzene in humans has been estimated to be over 22 hr (44); however, blood levels decay much faster than this after exposure. Sato cited blood level half-lives of 200 to 350 min for the latter portion of the decay curve (180-300 min) and much faster decay for the first 180 min.

Handy and Schindler (45) have derived a model for total body-burden of various pollutants using the pollutant concentrations, volume of air inspired (tidal respiratory volume times respiration frequency), absorption factor, and body weight. They assumed a continuous constant exposure, a biological half-life of 0.126 days, and, for lack of data at the time, 100 percent absorption. Using this model, they predicted a total body-burden of 2.02 mg/kg for continuous exposure to 25 ppm. Sato (8) found ~0.2 mg/kg after a 2-hr exposure. These numbers are reconcilable if the Handy-Schindler model uses 30 to 50 percent as the absorption rate and the 2-hr exposure used by Sato is extrapolated to steady state for which the model was derived. If these relations are extrapolated to very low benzene exposure and blood levels correspond to the body-burden, some estimate of potential blood levels may be made. Blood levels of 0.2-0.4 ng/mL would be anticipated for continuous exposure to 10 ppb, a high ambient air level.

MECHANISM OF BENZENE BIOTRANSFORMATION

The proposed scheme for the hepatic oxidative metabolism is depicted in Figure 15. The metabolic sequence begins with the hydroxylation of benzene by the heptatic mixed function oxidase to the benzene oxide. This epoxide may then undergo a number of metabolic conversions. The epoxide may be converted by the glutathione-S-epoxide transferase to yield phenylmercapturic acid. Alternatively, the epoxide hydrase may catalyze the enzymatic conversion of the epoxide to the diol, which then may be dehydrogenated to catechol. However, the predominant pathway for the metabolism of the epoxide may be its spontaneous rearrangement to the phenol. Both the phenol and catechol may be converted to the corresponding quinol, followed by the conjugation with a number of reactants to form either phenylsulfate or phenylglucuronides.

Supportive evidence for the proposed oxidative metabolism of benzene have come from both *in vivo* and *in vitro* studies (41,44,46,47). Microsomal preparations from mice, rats, rabbits, and dogs are capable of catalyzing both the hydroxylation of benzene and the subsequent conjugation reactions to yield either phenylsulfate or phenylglucuronide (44,47). In addition, Gerina et al. (46) have reported that benzene oxide can rearrange spontaneously to yield the phenol in the presence of mammalian hepatic microsomes. However, attempts to trap the benzene oxide intermediates after incubation of ^{14}C benzene with rabbit liver microsome in vitro have failed and may reflect the transient nature of the intermediate, which has a half-life of about 2 min in aqueous solution (48).

Moreover, the efficiency of the hepatic mediated oxidative metabolism of benzene can be markedly altered by chemical inducers and inhibitors. Pretreatment of animals with SKF-525A, an inhibitor of microsomal enzymes, prior to benzene administration can depress both phenol and glucuronide formation in rats. Alternatively, treatment of animals with phenobarbital induces the content of cytochrome P450, the dominant heme protein in biological hydroxylation reactions, and a number of hepatic microsomal enzymes (45). Liver microsomes from pretreated animals are capable of metabolizing benzene more efficiently, increasing severalfold the concentration of conjugated and unconjugated phenols over control animals (47). More importantly, these researchers indicate that phenobarbital-treated rats exhibit a greater resistance to leukopenic action of benzene.

The molecular site of benzene hematotoxicity is still uncertain. Although benzene is found to disrupt both DNA and RNA synthesis, the interruption appears after toxicity is manifest (48). At the translational level, benzene metabolism in animals has been associated with the disaggregation of polysomes to smaller aggregates in rabbit reticulocytes. This effect may be reversed by addition of hemin (37,48). Freedman (49) has proposed that the primary toxic effect of benzene at the cellular level is probably the

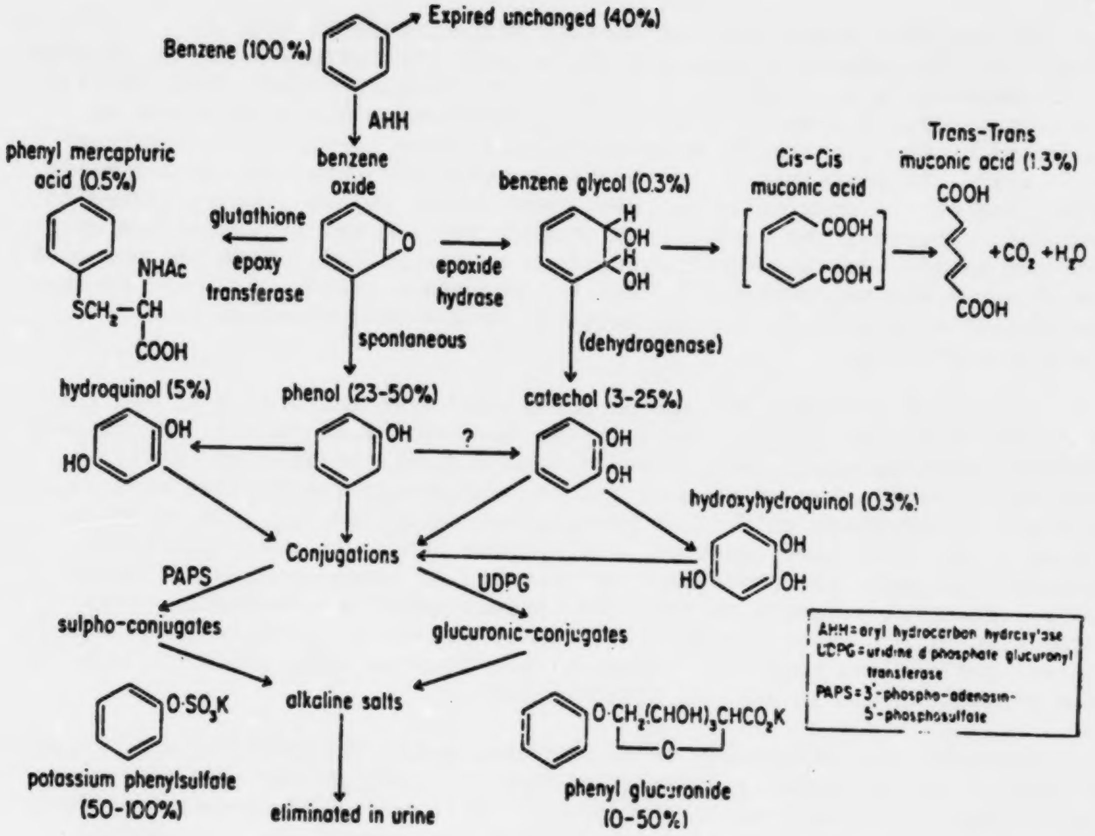

Benzene (100 %)
Expired unchanged (40%)
AHH
benzene oxide
phenyl mercapturic acid (0.5%)
glutathione
epoxy transferase
NHAc
SCH₂–CH
COOH
epoxide hydrase
benzene glycol (0.3%)
H
OH
H
OH
Cis-Cis muconic acid
COOH
COOH
Trans-Trans muconic acid (1.3%)
COOH
+CO₂ +H₂O
COOH
spontaneous
(dehydrogenase)
hydroquinol (5%)
phenol (23-50%)
catechol (3-25%)
HO
OH
OH
?
OH
OH
hydroxyhydroquinol (0.3%)
Conjugations
HO
OH
OH
PAPS
UDPG
sulpho-conjugates
glucuronic-conjugates
alkaline salts
O·SO₃K
O·CH₂(CHOH)₃CHCO₂K
O
potassium phenylsulfate (50-100%)
eliminated in urine
phenyl glucuronide (0-50%)
AHH = aryl hydrocarbon hydroxylase
UDPG = uridine d phosphate glucuronyl transferase
PAPS = 3'-phospho-adenosin-5'-phosphosulfate

Figure 15. Pathways of benzene metabolism and elimination.

© 1977, *Journal of Toxicology and Environmental Health*, used by permission of Hemisphere Publishing Corporation inhibition of reticulocyte heme synthesis at or before the aminolevulinic acid (ALA) synthesis step. Heme synthesis appears to be maximal in the earliest precursor cells and to decrease with cell maturity, while globin synthesis increases with cell maturity. These researchers suggest that heme and globin syntheses are interdependent and that heme synthesis may be necessary to increase intracellular hemin concentration to a level to allow erythropoiesis to proceed. Benzene, because of its lipid solubility, may prevent heme synthesis in early bone marrow cells, leading to development of aplastic anemia in treated animals. Induction of ALA synthesis is related to several hormones and the inhibition of this reaction by benzene may explain the higher susceptibility to benzene-induced hematotoxicity in the female as compared to male animals (37). These findings in rabbit reticulocytes, although important in deducing the hematotoxic mechanism, need to be interpreted and extrapolated with care to human clinical situations. More work with animals is required to determine the toxicity level of benzene in bone marrow, especially the mechanism of concentration, and its subsequent development to the pathological hematological conditions.

BENZENE TOXICOLOGY

Benzene Toxicity

The general effects of benzene toxicity are shown in Table 44. Clinical toxicity due to benzene exposure may be divided into two categories: acute toxicity and chronic toxicity. Acute benzene toxicity is generally associated with CNS stimulation, followed by depression and respiratory failure (50). These toxic effects in animals appear to be independent of the route of administration and require concentration(s) many times in excess of that to induce chronic toxic effects. Chronic benzene toxicity, however, leads essentially to a disorder of the hematopoietic system with the primary effect in animals localized to the bone marrow (37,50). Macrocytosis, characterized as appearance of giant abnormal red blood cells, may serve as an indicator of benzene-induced hematotoxicity. Another common clinical sign of chronic benzene toxicity is pancytopenia, defined as a decrease in circulating erythrocytes, granulocytes, and platelets (see Table 45). The marked leukopenia is probably due to the shorter lives of the peripheral leukocytes in benzene-treated animals. These leukocytes may also exhibit altered function such as a decrease in phagocytic function and in alkaline phosphatase activity. Other chronic effects noted in animals include changes in levels of urine and blood porphyrin and aminolevulinic acids, suggestive of altered heme synthesis. Severe pancytopenia is generally associated with aplastic anemia, a condition characterized by a decrease in the number of hematopoietic precursor cells within the bone marrow. The putative metabolite(s) of benzene responsible for the hematotoxic effects is still uncertain. Young animals and female animals appear to be more susceptible to benzene toxicity (see Table 46), but these findings need to be verified. In general, available data on dose-responsive hematotoxic effects in animals are difficult to assess because of variation in dose and route of administration, age and species of animals, and in the parameter of toxicity studied.

Table 44. GENERAL EFFECTS OF BENZENE INTOXICATION

Authors	Year	Treatment	Species	Comment
Carpenter et al.	1944	Inhalation 35,000-45,000 ppm	Rabbits	Slight anesthesia in approximately 4 minutes; deaths occurred in 22 to 71 minutes, indicating wide differences in tolerance to benzene narcosis
Gerarde and Ahlstrom	1966	Sc injection, 1 mL/kg x 14	Rats	Leukopenia
Hough and Freeman	1944	Inhalation 600-1,000 ppm,	Dogs	Leukopenia, shorter survival times
Jenkins et al.	1970	Inhalation, 817 ppm x 30 days	Rats, Guinea pigs, Dogs	Slight drop in WBC count
Nahum and Hoff	1934	Inhalation, air saturated with benzene vapor	Cats, Monkeys	Ventricular extrasystole or periods of ventricular tachycardia which occasionally terminated in ventricular fibrillation
Sidorov	1972	Inhalation, periodic or continuous	Mice, Rats, Guinea pigs, Rabbits	LD_{50} studies on joint action affected more by continuous exposure than by periodic
Withey and Hall	1975	Intubation	Rats	LD_{50} studies on joint action of benzene and perchloroethylene. Effect was additive.

(continued)

Table 44 (continued)

Authors	Year	Treatment	Species	Comment
Wolf et al.	1956	Inhalation, 80-88 ppm for 6 months Oral, 1 mg/kg/day for 6 months	Rats, Guinea pigs, Rabbits	Milk leukopenia, splenic and testicular degeneration
Yakushevich	1973	Inhalation, continuous and periodic	Rats	Continuous inhalation caused more pronounced effects than periodic inhalation

Source: Leong, B. K. J., Experimental Benzene Intoxication, J. Tox. Environ. Health Supplement, 2, (1977), pp. 46.

Sc = subcutaneous.

Table 45. BONE MARROW CHANGES DUE TO BENZENE INTOXICATION

Authors	Year	Treatment	Species	Comment
Das et al.	1969	Sc injection	Guinea pigs	Leukocytosis followed by leukopenia and granulocytopenia in 6-8 days.
Das et al.	1969	Repeated sc injection	Guinea pigs	Removal bone marrow hypoplasia.
Gerarde	1956	Sc injection 1 mL/kg x 14 days	Rats	Leukopenia, involution of the spleen and thymus, and a decrease in femoral marrow nucleated cell count and nucleic acid. The injury was reversible.
Koike et al.	1959	1 mL/kg daily x 5 weeks, or 2 mL/kg daily x 3 weeks	Rats	A rapid fall in femoral marrow nucleated cell count and in DNA-P content per dry weight of bone marrow.
Moeschlin and Soeck	1967	Sc injection 2 mL/kg x 1	Rabbits	Severe inhibition of DNA-synthesis in bone marrow cells.
Steinberg	1949	≈1 mL benzene per rabbit	Rabbits	Only primitive reticular cells during regeneration. Benzene inhibits cell division and maturation.

Source: Leong, B. K. J., Experimental Benzene Intoxication, J. Tox. Environ. Health Supplement, 2, (1977), pp. 51.

Sc = subcutaneous.

Table 46. EFFECTS OF AGE AND SEX ON BENZENE TOXICITY

Authors	Year	Treatment	Species	Comment
Avilova	1971	Technical details not available	Rats	Young rats were affected more severely and for a longer period than older rats
Desoille et al.	1961	Sc injection of benzene, 0.1 g/kg	Rabbits	Female rabbits or male rabbits previously feminized by castration or injection of estrogen were more sensitive to the leukopenic effect of benzene
Desoille et al.	1962	Sc injection of benzene, 0.1 g/kg	Rabbits	Gestation has no effect on the leukopenic effect of benzene
Gadaskina et al.	1973	Technical details not available	Rabbits	Young rabbits are more sensitive to benzene poisoning, probably because of less efficient conjugation with salfuric and glucuronic acids
Ito	1962	Inhalation	Mice	1 hour $LC_{50} \cong 14{,}500$ ppm for both male and female mice
Ito	1962	Inhalation	Rats	Hematological changes appeared faster in females than in males
Ito	1962	Inhalation exposure, daily for 2 months	Rats	Ovariectomized or testosterone-treated female rats showed early development of hematological changes

(continued)

Table 46 (continued)

Authors	Year	Treatment	Species	Comment
Kimura et al.	1971	Oral	Rats	Benzene is more toxic orally to 14-day-old rats than young adult and older adult rats. The LD_{50} values were 3.4, 3.7, and 4.4 mg/kg, respectively.
Manyashin et al.	1968	Intubation	Rabbits	Young rabbits were more sensitive than older rabbits. Young rabbits excreted more phenol than older rabbits
Minai	1967	Sc injection for 5 days	Rabbits Hamsters, Rats, Mice	Rats are more sensitive and hamsters are least sensitive to benzene poisoning

Source: Leong, B. K. J., Experimental Benzene Intoxication, J. Tox. Environ. Health, Supplement, 2, (1977), pp. 60.

Sc = subcutaneous.

The contribution of these chronic toxic effects to development of leukemia, defined as a neoplastic condition arising from proliferation of white blood cells or precursors in blood and/or in bone marrow, remains uncertain (6,50). (See Table 47). The changes in leukocyte numbers and functions after benzene exposure in animals are likely to alter the immune system and may increase their susceptibility to development of leukemia. However, whether benzene, its metabolite product(s), and/or severe damage to the bone marrow cells act as the initiator(s) or promotor(s) of leukemia is unknown. While acute myelogenous leukemia and related disorders have been strongly linked to benzene exposure in humans by a number of epidemiologic studies (6,36,50), attempts to induce leukemia in experimental animals have not been very successful (50). Table 47 presents a representative sample of such attempts to induce tumors in experimental animals.

BENZENE-INDUCED MUTAGENICITY AND CHROMOSOMAL ABNORMALITIES

The mutagenicity of benzene has been tested with the Ames/Salmonella mutagenesis bioassay which detects carcinogens as mutagens (40). The specific Salmonella strains employed include TA98 (which detects frame shift mutagens) and TA100 (which detects base-substitution mutagens). No mutagenic activity was detected. Attempts to increase the sensitivity of the bioassay by addition of epoxide hydrase inhibitor, use of pre-incubation procedure, and the addition of S-9 microsome from bone marrow of methylcholanthrene-treated rats were all unsuccessful in detecting mutagenic activity.

Atypical cell nuclei, altered DNA metabolism and cell division, and increased chromosome abnormalities are common cytologic features found in cultured cells and in animals exposed to benzene (40,50,51). Wolman (51) notes that giant nuclei, especially in erythroid precursor cells, have been found in newts, rabbits, and humans. Moreover, dividing erythroblasts from newts treated with benzene exhibit higher incidence of amitotic arrests and chromosomal anomalies at various stages of mitosis than control animals. Such chromosomal abnormalities may lead subsequently to unequal nuclear division, polynucleated cells, and atypical nuclei.

Apart from these nuclear structural changes, other chromosomal aberrations and altered DNA synthesis have been demonstrated in cultured human lymphocytes and HeLa cells after benzene treatment *in vitro* and in cultured rat and rabbit bone marrow cells after treatment *in vivo* (40,51) (see Table 48). For example, bone marrow cells of rats exposed to benzene over a period of 12 days exhibit a higher incidence of chromosomal breaks and gaps (51). Similarly, cultured human leukocytes treated with 1-2 x 10 ^{3}M benzene are shown to have a higher incidence of chromosomal breaks and gaps. Moreover, the addition of radiation (100 rad) and benzene (1-2 x 10 ^{3}M) to these cells has a synergistic effect, enhancing the number of chromosomal aberrations; the additive effect is presumably attributed to benzene-induced inhibition of DNA repair of radiation-induced chromosome breaks. At higher benzene concentration, these cultural cells become more susceptible to inhibition of DNA synthesis (manifest as a decrease in tritiated thymidine uptake) (40). The reduction in DNA synthesis in these cells at higher benzene concentrations complicates the interpretation of dose-dependency to incidence of chromosomal breaks and whether these chromosomal changes should be classified

Table 47. POSSIBLE LEUKEMOGENIC AND TUMORIGENIC EFFECTS OF BENZENE

Authors	Year	Treatment	Species	Comment
Amiel	1960	Sc injections of 0.001 mL weekly from age 1 month until death	Five strains of mice	No leukemogenic or aplastic effects were observed
Hamaguti and Yosida	1938	0.001 mL weekly	Mice	Developed "preleukemic" state in lymph nodes, spleen, and liver
Hiraki et al.	1963	Sc injections	Mice	Developed subcutaneous sarcomas
Kirschbaum and Strong	1942	Sc injections, 0.001 mL weekly	High leukemia F strain mice	Six of 20 treated mice developed leukemia; 29 of 212 control also developed leukemia
Laerum	1973	Benzene was painted on skin twice weekly for life	Hairless mice	Frequency of spontaneous reticulum cells neoplasma was the same as in unpainted control
Lignac	1932	0.001 mL benzene in 0.1 mL olive oil for 17-21 weeks	Mice	Eight of 33 mice developed lymphoblastoma
Ward et al.	1975	Repeated six injections for 104 weeks	C57BL/6N	No evidence of carcinogenic effects

Source: Leong, B. K. J., Experimental Benzene Intoxication, J. Tox. Environ. Health, Supplement, 2, (1977), pp. 55.

Sc = subcutaneous.

Table 48. POSSIBLE MUTAGENIC AND TERATOGENIC EFFECTS OF BENZENE

Authors	Year	Treatment	Species	Comment
Dobrokhotov	1972	Sc, 200 mg/kg/day x 12 days	Rats	Chromosomal changes in bone marrow cells
Kissling and Speck	1972	Sc, 0.2 mL/kg/day for 18 wks	Rabbits	Chromosomal aberrations (breaks and gaps) were present in bone marrow cells
Matsushita	1966		Rats	Mitotic inhibition in metaphase stage and chromosomal damage, probably due to inhibition of the nucleoprotein metabolism of the nucleic acid synthesis
Phillip and Jensen	1970	Sc, 2 mL/kg	Rats	Chromatid aberrations of chromosome of bone marrow at 12 and 24 hours postinjection
Pollini et al.	1965	Inoculated with 0.005, 0.003, 0.0015 mL. Examined after 60, 64, and 68 hours of incubation	Chick embryo	All doses inhibited mitosis of embryo hemopoietic cells
Watanabe et al.	1970	Sc injection, 3 mL/kg on 11th to 15th gestation day	Mice	Cleft palate, agnathia, and micrognathia were observed more frequently in pregnant mice injected with benzene on 13th day

as a mutational or toxic event (51). In addition, the inclusion of both breaks and gaps as signs of chromosome aberration by many researchers may inflate the aberration rates since the formation of chromosomal gaps may be inducible during preparation of the chromosomal sample (51). Thus, while the association between benzene exposure and development of chromosomal abnormalities has been demonstrated, in many animal species, the dose-response relationship remains unclear.

PROBLEMS ASSOCIATED WITH EXTRAPOLATION OF ANIMAL DATA TO HUMANS

The use of similar animal systems to predict the toxicological behavior of xenobiotics in humans has been the cornerstone of most toxicological studies; but there are problems when laboratory toxicity data are extrapolated to man. A basic question is whether high dose testing with animals (for both acute and chronic benzene exposure) is a good measure of human health effects expected from either intermittent acute exposure or chronic low dose exposure. The findings that the intervals between intermittent benzene exposures enable the animal to recover from the toxic effects further complicates the estimation of human risk (52). Another problem has been the lack of information quantifying the relationship between benzene dose and incidence of toxic effects. Some of the difficulties in assessing the dose-response relationship have already been discussed in this report. Robert Dixon, Head of the Environmental Toxicology Division at NIEHS, has suggested that toxicological testing with animals should meet certain guidelines (53). Foremost among the recommendations is that the maximum tolerable dose should exhibit no overt toxicity; should not shorten the life span of the test animal(s); and should not decrease the expected weight gain during the animal's lifetime. Another is that the test dose should not saturate the pharmacokinetic processes nor overwhelm the animal's adaptive mechanisms. Whether many of the experimental studies investigating benzene toxicity in animals fulfill the guidelines is uncertain. Thus, extrapolation of laboratory benzene toxicity data to humans must be interpreted with caution.

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APPENDIX A

SAMPLING AND ANALYTICAL PROTOCOLS FOR BENZENE IN AIR, WATER, BLOOD BREATH, AND URINE

SAMPLING AND ANALYSIS OF BENZENE IN BREATH AND AIR

PRINCIPLE OF METHOD

Recovery of volatile organics from Tenax GC is accomplished by thermal desorption and purging with helium into a liquid-nitrogen-cooled nickel capillary trap (1-3). The vapors are then introduced into a high resolution glass capillary gas chromatographic column where the constituents are separated from each other (2,4). Quantification of the benzene in the sample is accomplished by gas chromatography/flame ionization detection (GC/FID). Confirmation of a portion of the samples selected on the basis of availability of replicates and dispersal throughout the set is made by gas chromatography/mass spectrometry (GC/MS). The thermal desorption inlet-manifold used with both GC/FID analysis and GC/MS analysis is shown in Figure A-1. The overall analytical system for the GC/MS analysis is shown in Figure A-2.

RANGE AND SENSITIVITY

The linear range for this analysis is defined on the lower extreme by the background of the Tenax cartridges. The upper limit is defined by the capacity of the capillary column, a somewhat variable factor depending upon individual column characteristics. Typically, support coated open tubular (SCOT) columns have a wider dynamic range, about 10^4, but lower resolution. The wide bore (0.55 mm i.d.) wall-coated open tubular (WCOT) columns have about a 10^3 linear dynamic range.

The detection limit for ambient air is determined by the Tenax cartridge background, which is a function of the original cleanup of the cartridge and its storage time and conditions. Freshly cleaned cartridges typically have <20 ng each of benzene (0.6 $\mu g/m^3$ for a 30-L air sample). The control samples from the two study sites contained 50 ± 40 ng (1.7 $\mu g/m^3$ for 30-L air sample) showing some storage effect. Breath samples have an additional background due to the benzene in the breathing air used in the experiment. Depending upon the air purity, sampling conditions, and storage background, values of 0.3 to 4.2 $\mu g/m^3$ may be obtained.

INTERFERENCES

Extremely high levels of other hydrocarbons can degrade the separation of benzene from other constituents with GC/FID. This is not a problem with GC/MS where specific ions can be monitored.

PRECISION AND ACCURACY

Replication of standard cartridges is generally ±10%. Air control samples that have been subjected to the rigors of transportation and storage show recoveries averaging 75% with a standard deviation of 19% (26% relative standard deviation). Breath controls averaged 82 ± 22% recovery (27% relative standard deviation).

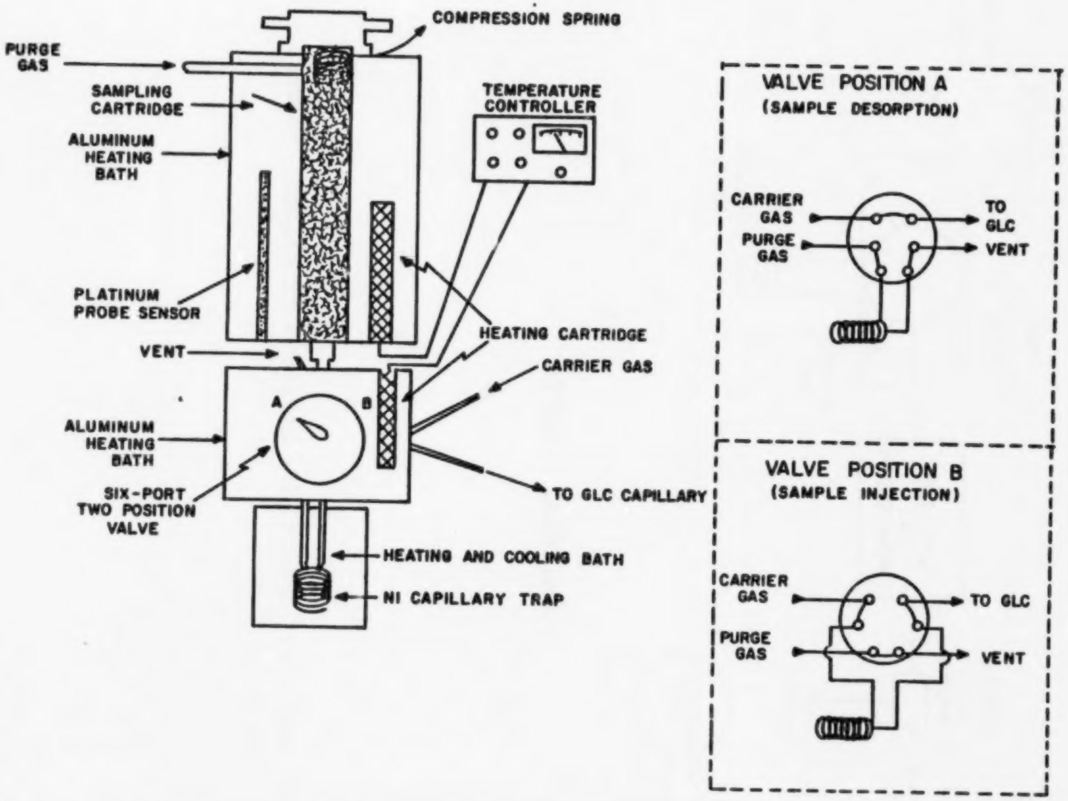
COMPRESSION SPRING
PURGE GAS
SAMPLING CARTRIDGE
ALUMINUM HEATING BATH
TEMPERATURE CONTROLLER
PLATINUM PROBE SENSOR
HEATING CARTRIDGE
VENT
CARRIER GAS
A
B
ALUMINUM HEATING BATH
SIX-PORT TWO POSITION VALVE
TO GLC CAPILLARY
HEATING AND COOLING BATH
NI CAPILLARY TRAP
VALVE POSITION A
(SAMPLE DESORPTION)
CARRIER GAS
PURGE GAS
TO GLC
VENT
VALVE POSITION B
(SAMPLE INJECTION)
CARRIER GAS
PURGE GAS
TO GLC
VENT

Figure A-1. Thermal desorption inlet-manifold.

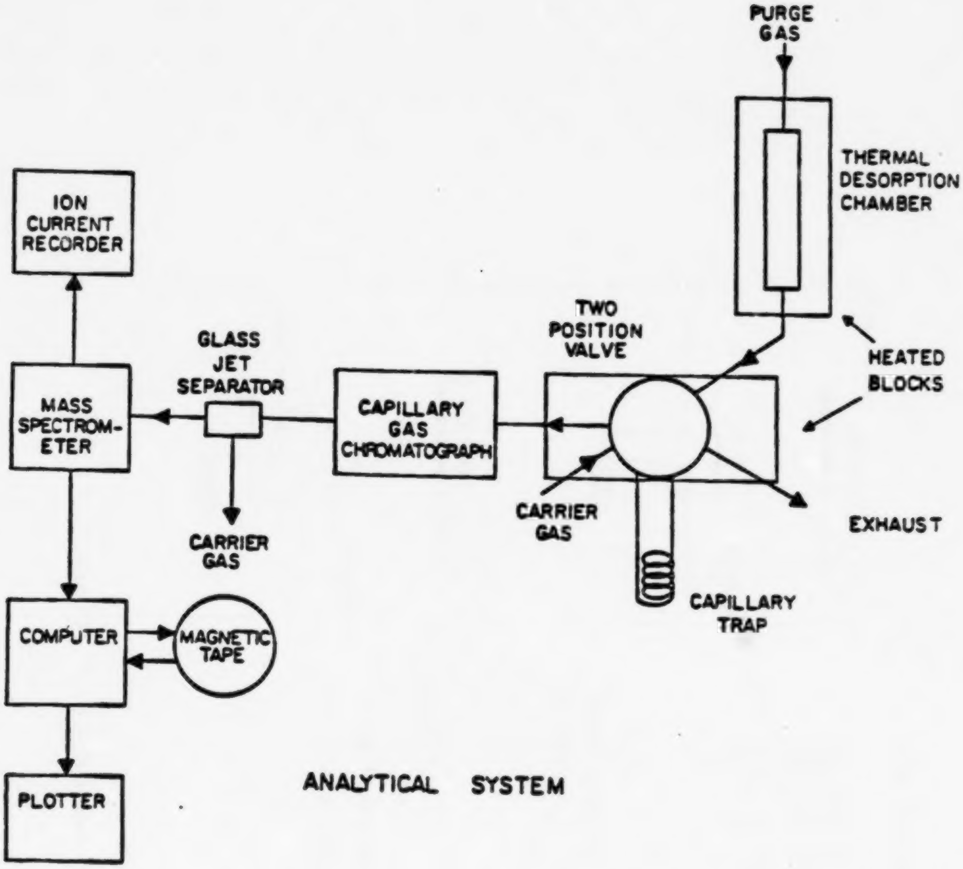
PURGE GAS
THERMAL DESORPTION CHAMBER
ION CURRENT RECORDER
TWO POSITION VALVE
GLASS JET SEPARATOR
HEATED BLOCKS
MASS SPECTROM-ETER
CAPILLARY GAS CHROMATOGRAPH
CARRIER GAS
EXHAUST
CARRIER GAS
CAPILLARY TRAP
COMPUTER
MAGNETIC TAPE
PLOTTER
ANALYTICAL SYSTEM

Figure A-2. Analytical system for analysis of organic vapors in ambient air.

APPARATUS AND REAGENTS

Collection of Samples

Personal Monitor Pump--

A personal monitor pump (MSA Co. -- Model C-200) is used for air sample collection. Flow rates are adjusted to ~0.05 L/min for an 8-hr collection period. Flows are adjusted such that a total volume of ~0.024 m^3 air is sampled for a given collection period.

Spirometer--(See Appendix B.)

Sampling Cartridges--

The sampling tubes are prepared by packing a 10-cm long by 1.5-cm i.d. glass tube containing 8 cm of 35/60 mesh Tenax GC with glass wool in the ends to provide support (2,9). Virgin Tenax (or material to be recycled) is extracted in a Soxhlet apparatus for a minimum of 18 hrs each time with methanol and *n*-pentane prior to preparation of cartridge samplers (2,9). After purification of the Tenax GC sorbent and drying in a vacuum oven at 120° C for 3 to 5 hrs at 28 in of water, all the sorbent material is meshed to provide a 35/60 particle size range. Meshing and all further cartridge preparation is conducted in a "clean" room. Cartridge samplers are then prepared and conditioned at 270° C with helium flow at 30 mL/min for 30 min. The conditioned cartridges are transferred to Kimax® (2.5 cm x 150 cm) culture tubes, immediately sealed using Teflon®-lined caps and cooled. This procedure is performed to avoid recontamination of the sorbent bed (2,10).

Inlet Manifold

An inlet manifold for thermally recovering vapors trapped on Tenax sampling cartridges is used and is shown in Figure A-1 (1-4).

Gas Chromatograph

A Varian 3700 gas chromatograph with a glass capillary column is interfaced to the inlet manifold above. This analytical system is presented schematically in Figure A-1.

Mass Spectrometer/Computer

A Varian MAT CH-7 mass spectrometer capable of a resolution of 2,000 equipped with single ion monitoring capability is used in tandem with a Varian 1700 gas chromatograph and interfaced to a Varian 620/L computer (Figure A-2).

A glass jet separator is employed to interface the glass capillary column to the mass spectrometer on the Varian MAT CH-7 GC/MS/COMP system. The separator is maintained at 240° C (2).

Reagents and Materials

All reagents used are analytical reagent grade. All solvents are "distilled in glass" (Burdick & Jackson) or are redistilled before their use.

Solvents -- methanol, pentane, acetone.

Sorbent -- Tenax GC (35/60 mesh) is obtained from Alltech Associates. The same pretested lot is used throughout.

PROCEDURE

Collection of Benzene in Ambient Air

The volume of air which can be sampled for benzene is limited by the breakthrough volume of benzene on the Tenax cartridge. At normal ambient temperatures, the sample volume is limited to 30 to 35 L of air. This volume limitation must be observed for both air and breath samples.

Collection of Benzene in Breath

The method for collection of benzene in breath and the specialized equipment required is described in Appendix B.

Desiccation of Tenax Cartridges from Breath Samples

Breath is an especially humid air and as such considerable water accumulates on the cartridges. Since water frequently interferes with the transfer of sample from the cartridge to a gas chromatograph (GC) capillary trap, a desiccation step is highly desirable. To establish that desiccation can be performed without loss of sample, Tenax cartridges were first loaded with high humidity air and spiked with benzene. They were then desiccated over calcium sulfate (precleaned in a muffle furnace at 400° C for 1 to 2 hrs. Thermal desorption of these cartridges indicated recovery after desiccation was 93.4%. (Relative standard deviation for 4 determinations was 3.8%.)

Analysis of Samples

The instrumental conditions for the analysis of benzene on the sorbent Tenax GC sampling cartridge is shown in Table A-1. The thermal desorption chamber and the six-port Valco valve are maintained at 250° C and 220° C, respectively. The helium purge gas through the desorption chamber is adjusted to 15-20 mL/min. The nickel capillary trap on the inlet manifold is cooled with liquid nitrogen. In a typical thermal desorption cycle, a sampling cartridge is placed in the preheated desorption chamber and the helium gas is channeled through the cartridge to purge the vapors into the liquid nitrogen capillary trap [the inert activity of the trap has been shown in a previous study (4,8)]. After the desorption has been completed, the six-port valve is rotated and the temperature on the capillary loop is rapidly raised (greater than 100°/min); the carrier gas then introduces the vapors onto the high resolution GC column. The glass capillary column is temperature-

Table A-1. OPERATING PARAMETERS FOR THERMAL DESORPTION GC/FID ANALYSIS OF BENZENE

Parameter	Setting
Inlet-manifold	
desorption chamber	250°C
valve	250°C
capillary trap - minimum	-196°C
- maximum	250°C
thermal desorption time	7 min
purge rate (He)	30 mL/min
GC	
108 M glass SCOT SE-30	45°C initial 1°/min
Nitrogen carrier gas flow rate	4.0 mL/min
47 M glass WCOT-SE-30/$BaCO_3$	50°C initial for 3 min then 4°/min to 200°C
Helium carrier gas flow rate	2.1 mL/min

programmed as indicated. After all the components have eluted, the column is cooled to ambient temperature and the next sample is processed (2).

Quantitation

Quantitation of benzene is accomplished by comparing peak areas at the benzene retention time to peak areas from cartridges loaded with known amounts of benzene from a permeation system (5,6).

$$\text{Benzene concentration } (\mu g/m^3) = \frac{A_{unk}/g_{std}}{A_{std}/V_{unk}}$$

where A_{unk} is the area of the benzene peak in the sample,
A_{std} is the area of the benzene peak in the standard(s),
g_{std} is the amount of benzene added to the standard (μg),
V_{unk} is the volume of air or breath collected (m^3).

QUALITY ASSURANCE PROGRAM

Reagent and Glassware Control

Reagent and glassware control is required to minimize contamination. Sample containers, glassware, etc., are cleaned with Isoclean®, rinsed with distilled/deionized water and heat treated at 450°-500° C to insure the removal of all traces of organic compounds.

Quality Control Samples

Blank sampling cartridges and control cartridges loaded with known amounts of benzene are prepared for each sampling trip. The total number of cartridges dedicated to blanks and controls is greater than 10% of the maximum number of field samples to be collected. A portion of the samples is designated "lab blanks/controls" and remains in the laboratory; another portion is designated "field blanks/controls" and is carried to the field in the same containers as the sample cartridges. This procedure not only provides a check on possible contamination during transport and storage, but also allow calculation of overall recoveries during the storage and analysis phases.

Blank samples for the breath sampling and analysis are generated in the field and in the laboratory by pumping 0.07 m^3 of air through the spirometer with the mouthpiece plugged and collecting two parallel blank cartridges. Controls were generated in the same way except that the cartridges were spiked with a solution of benzene in methanol before sampling.

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SAMPLING AND ANALYSIS OF BENZENE IN DRINKING WATER

PRINCIPLE OF THE METHOD

Two samples of drinking water are collected at each participant household. The first is the initial water flow and the second is the water collected after 3 min of maximum purge of the water lines. As a screen, water samples are composited such that benzene present at >1 µg/L would be detected in the composite. Any elevated values can then be evaluated individually.

SAMPLE COLLECTION

At each participant household, two samples of cold tapwater are collected in 120-mL precleaned glass bottles from the kitchen tap or source commonly used for drinking and/or cooking. The first sample is taken immediately upon turning on the water, without flushing; the second sample is taken after the water has been allowed to run for 3 minutes. Time is measured using a stopwatch.

COMPOSITING OF WATER SAMPLES

Aliquots of two or three water samples are mixed and an aliquot of the composite analyzed.

SAMPLE ANALYSIS

The water samples are analyzed by the Guidelines Establishing Test Procedures for the Analysis of Pollutants, Purgeables-Method (624) [1] using GC/FID for screening purposes.

QUALITY ASSURANCE PROGRAM

Reagent and Glassware Control

Reagent and glassware control is required to minimize contamination. Sample containers, glassware, etc., are cleaned with Isoclean®, rinsed with distilled-deionized water, and heat treated at 450°-500° C to insure removal of all traces of organic compounds.

Quality Control Samples

Blank water and control water spiked with known amounts of benzene are prepared for each sampling trip. The total number of cartridges dedicated to blanks and controls is greater than 10% of the maximum number of field samples to be collected. A portion of the samples is designated "lab blanks/controls" and remains in the laboratory; another portion is designated "field blanks/controls" and is carried to the field in the same containers as the samples. This procedure not only provides a check on possible contamination during transport and storage, but also allows calculation of overall recoveries during the storage and analysis phases.

REFERENCES

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SAMPLING AND ANALYSIS OF BLOOD AND URINE

PRINCIPLE OF THE METHOD

A blood or urine sample is equilibrated at 37°C with an air space of determined volume until equilibrium is attained. The entire headspace is then purged into a cryogenic trap which can be placed in line with a GC as a sample loop and heated. In this manner, the recovery is determined by the partition between fluid and air and avoids the many artifacts and other problems introduced by purging (i.e., foaming, precipitation occlusion, and sorbent background).

RANGE AND SENSITIVITY

The range is limited by the limit of detection on one extreme and by the chromatographic capacity of the capillary on the other or $\sim 10^4$. Minimum detectable concentration for the method is estimated to be 1.6 μg/L (95% confidence level).

INTERFERENCES

No interferences have been observed; however, high levels of other hydrocarbons in the sample could cause the benzene peak to be obscured.

PRECISION AND ACCURACY

Precision at 500 μg/L is 8% relative standard deviation increasing to 33% at 1.8 μg/L. Recovery of control samples spiked at 5 μg/L was 98%.

APPARATUS AND MATERIALS

1. A thermostated two-position, six-port valve with nickel capillary trap as indicated in Figure A-3.
2. A gas chromatograph with flame ionization detector.
3. Thermostated oven (37°C).
4. Glass capillary GC column, phase SE30.
5. Glass hypodermic syringes (10 mL) and needles.
6. Silicone rubber septum material.
7. Liquid nitrogen.
8. Ultrapure air (<0.1 ppm total hydrocarbon).

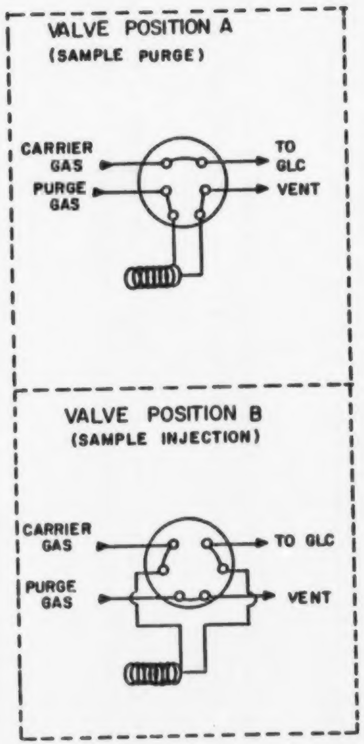
VALVE POSITION A
(SAMPLE PURGE)
CARRIER GAS
PURGE GAS
TO GLC
VENT
VALVE POSITION B
(SAMPLE INJECTION)
CARRIER GAS
PURGE GAS
TO GLC
VENT

Figure A-3. Six-port, two-position valve for the introduction of headspace samples.

PROCEDURE

Collection of Blood and Urine Sample

Blood samples are collected from selected participants from a brachial vein by venipuncture using a 10-mL Venoject tube. These blood samples are collected by experienced medical personnel using accepted medical procedures.

Urine samples are collected by the participants in a precleaned 120-mL wide-mouth bottle.

Analysis of Samples

Pre-equilibrate a 10-mL glass syringe at 37°C (>30 min), remove the needle from the syringe and inject 1.0 mL of blood or urine (sample, standard, or blank) into the syringe which has been sealed around the plunger with saturated lithium chloride. Adjust the volume to 10 mL by filling the syringe with "ultrapure" air, replace the needle on the syringe, and seal it by inserting it into a piece of silicone septum material. Incubate the entire syringe assembly at 37°C for 20 min. After the incubation, the needle is removed and the syringe is connected to the cryogenic trap via an 18-gauge needle. The total air space in the syringe is purged through the trap. An additional 1 mL of air is purged through the trap from another syringe. The latter step is to prevent sample holdup in the transfer lines to the trap.

At this point, the coolant (liquid nitrogen) is removed from the trap, the valve rotated, and the trap rapidly heated to 175°C. The GC operating parameters are given in Table A-2.

Calibration of the GC is obtained by analyzing blood spiked with known amounts of benzene and blood blanks under identical conditions to the sample.

Quantitation

Peak areas of benzene in unknown samples are compared to calibration curves generated with known amounts of added benzene. This results in the following relationship:

$$\text{Concentration of benzene } (\mu\text{g/L}) = \frac{A_{unk}/g_{std}}{A_{std}}$$

where A_{unk} is the peak area of the sample,
g_{std} is the amount of benzene added to the standard
A_{std} is the peak area of the standard.

VARIATIONS IN THE BLOOD ANALYSIS PROTOCOL

Pretest blood samples were analyzed using a glass GC column 285 x 0.2 cm packed with 2% OV-101 on Gas Chrom Q (100/120 mesh). The blood samples from Houston were analyzed on an SP-1000 (0.1%) on Carbopack C (80/100 mesh)

Table A-2. OPERATING PARAMETERS FOR GC/FID ANALYSIS OF BENZENE IN BLOOD AND URINE

Parameter	Value
Column	
47 M glass WCOT SE-30, $BaCO_3$	50°C initial for 3 min then 4°/min to 200°C
Helium carrier gas flow rate	2.1 mL/min

column, 200 x 0.2 cm. A photoionization detector (HNU, Inc.) was used as a detector; however, the sensitivity was less than that obtained with the method described above (~20 μg/L).

QUALITY ASSURANCE PROGRAM

Reagent and Glassware Control

Reagent and glassware control is required to minimize contamination. Sample containers, glassware, etc., are cleaned with Isoclean®, rinsed with distilled-deionized water, and heat treated at 450-500° C to insure the removal of all traces of organic compounds.

Quality Control Samples

Blank blood was obtained from several individuals who have low benzene exposure potential and the blood was pooled. Aliquots were placed in the same type of vials used for sample blood storage. Some of these aliquots were spiked with known quantities of benzene as controls. In total the number of aliquots is 10-20% of the expected number of blood samples. A portion of the samples is designated as "lab blanks/controls" and remains in the laboratory; another portion is designated "field blanks/controls" and is carried to the field in the same containers as the sample cartridges. This procedure not only provides a check on possible contamination during transport and storage, but also allows calculation of overall recoveries during the storage and analysis phases.

APPENDIX B

SPIROMETER FOR THE DETERMINATION OF BENZENE IN BREATH

SPIROMETER FOR THE DETERMINATION OF BENZENE IN BREATH

INTRODUCTION AND PRINCIPLE OF THE METHOD

Conkle et al. (1) have evaluated human breath for "normal" levels of various organics including benzene. They needed a multistage cryogenic trap for sample collection which was too cumbersome for field sampling so the spirometer described below has been designed.

There are several design criteria which must be met. Due to the low levels of benzene anticipated, the sample must be accumulated over a period of time. Since the subject breathes into the device for a period of time (up to 15 min), he/she must not be unduly discomforted while maintaining sample integrity. This comfort factor requires minimal back pressure (<2 mm of Hg). A Tenax cartridge used as an accumulator directly coupled to the exhaust valve exhibited too great a back pressure at normal respiratory flow rates of 7 L/min. Since transient flow rates may reach 10 times the average, an alternative design was considered. A collapsible reservoir such as a Tedlar bag was used between the subject and the cartridge(s) and the expired air drawn through the cartridge(s) by a metered pump. With an adequate volume in the bag, matching the pumping rate and the respiratory flow was relatively simple. The same low pressure differential had to be maintained for the inspired air, hence a similar bag arrangement was used to provide the subject with ultrapure air. The sampling apparatus is shown schematically in Figure B-1.

MATERIALS

1. Air cylinder-Zero 0.1® Air (Airco, Inc. Cat. No. 331-09926) with two-stage regular valve [all metal seals for low hydrocarbon background e.g., Airco Model 18-75 (CGA 590)].

2. Activated Carbon Filter (28.8 cm i.d. x 16 cm) with 1/2-in fittings.

3. Air Humidifier-Midget impinger (Lab Glass LG-6819-122) with ₸ 24/40 joint and 12/5 ball joints at entrance and exit; 250-mL Erlenmeyer with 24/40 joint; two 12/5 ground ball sockets (Lab Glass: LB-1045-110), two Size 12 pinch clamp for ball and socket joints (Lab Glass: LG-1045-102).

4. Bulkhead Quick Connects (2) [Body Assembly, Viton o-ring, 1/4 in stainless steel (Swagelok: SS-QC4-B1-400)].

5. Body and Stand for the Spirometer--A metal box 30 x 45 x 60 cm with a door in the top and openings for tubing and four sturdy legs to produce an overall height of 90 cm. The following fixtures are added to support the various components Flexframe® foot plates (2), Flexframe® rods (2 - 12 cm, 1 - 60 cm), Clamp holders (3), and a three-prong clamp.

6. Tedlar bags, 50-L capacity (2 minimum). The dimensions and configuration in the Tedlar bags are given in Figure B-2. Fittings necessary for each bag, Teflon® nut 7/16 x 20 straight thread (1), o-seal straight thread adapter [Swagelok: SS-401-A-OR], 1/4 in nut and ferrules,

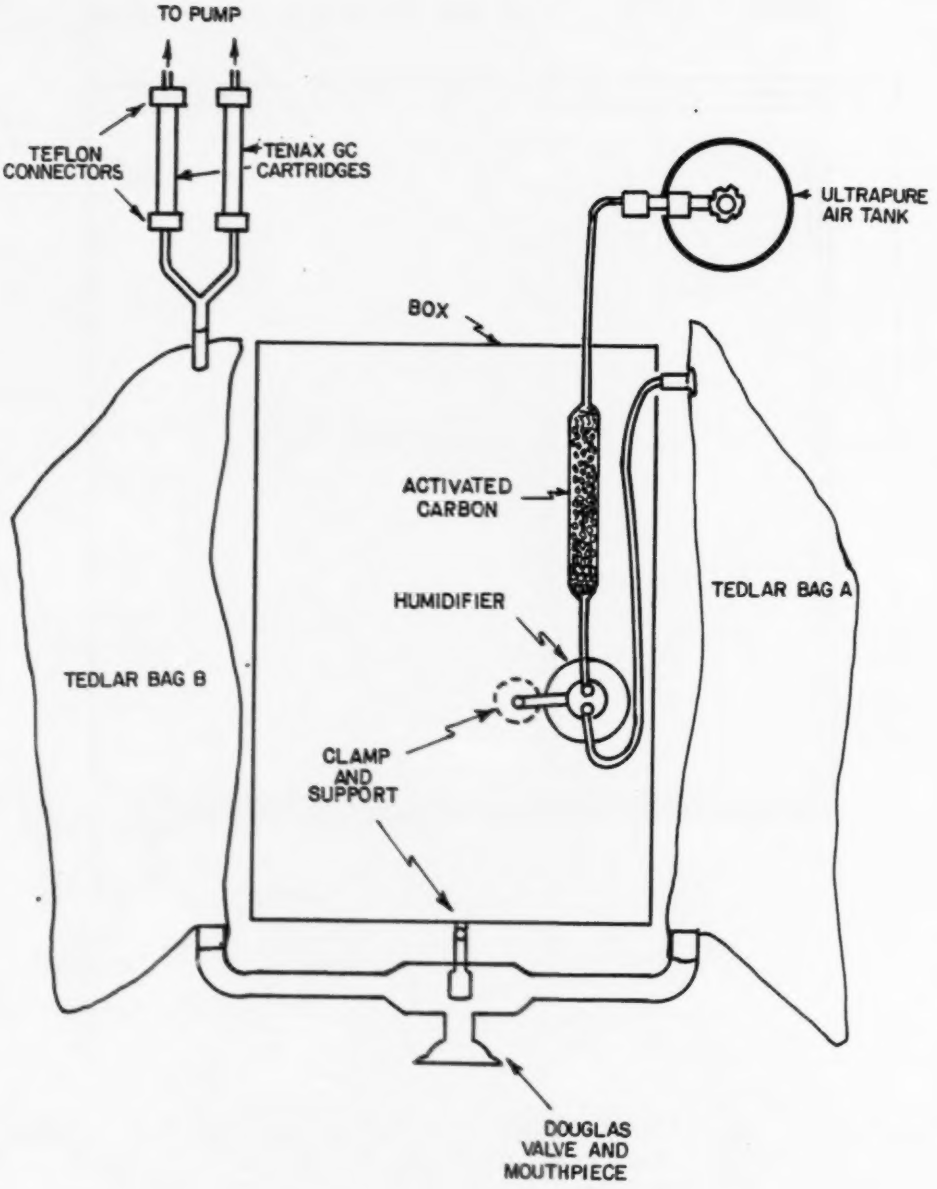
TO PUMP
TEFLON CONNECTORS
TENAX GC CARTRIDGES
ULTRAPURE AIR TANK
BOX
ACTIVATED CARBON
HUMIDIFIER
TEDLAR BAG A
TEDLAR BAG B
CLAMP AND SUPPORT
DOUGLAS VALVE AND MOUTHPIECE

Figure B-1. Schematic diagram of the spirometer.

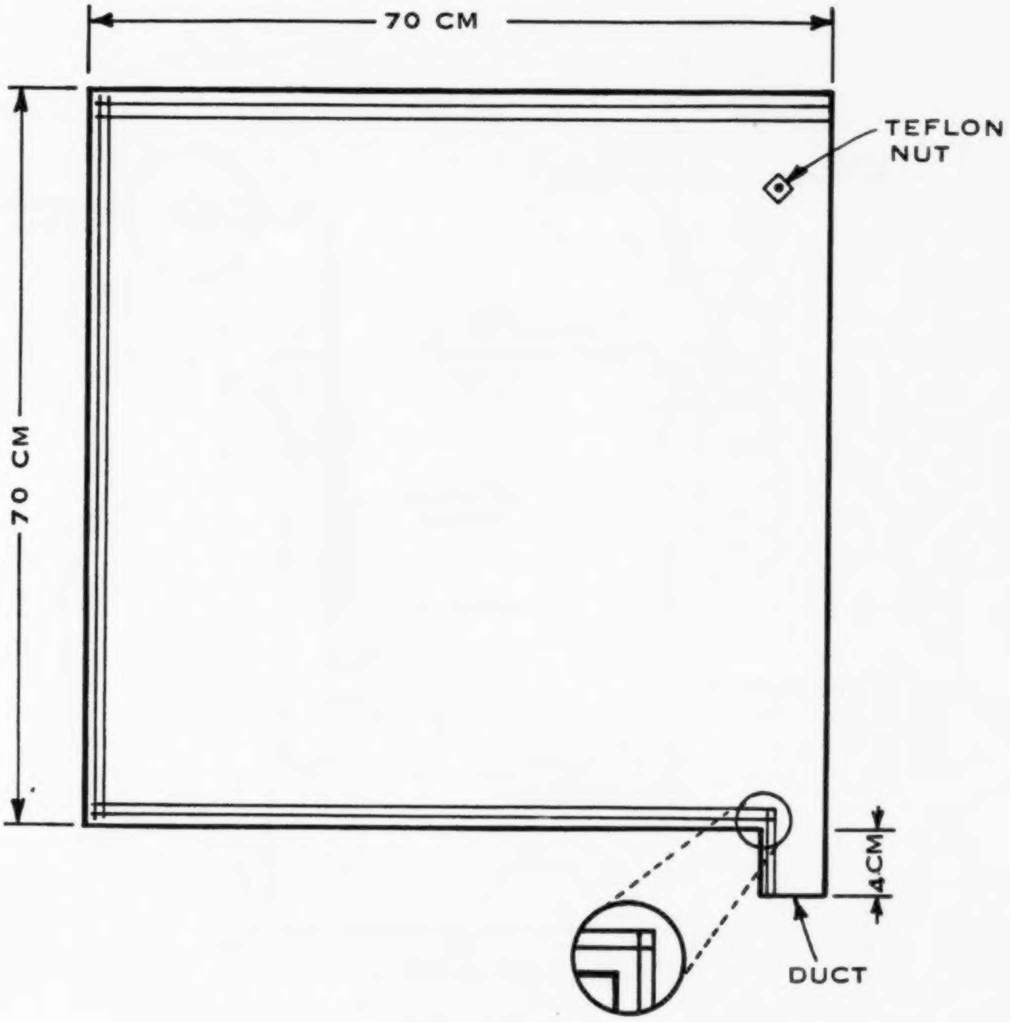
70 CM
70 CM
TEFLON NUT
4CM
DUCT

Figure B-2. Specifications for 50-L Tedlar® bag with duct. Opening to fit 2.5-cm pipe, tapering for better fit; standard Teflon nut for 7/16-2 straight thread sealed inside.

stainless steel, 1/4-in stainless steel quick connect with shut-off [Swagelok: SS-QC4-D-400].

7. Clamp, pinch type (1).
8. Douglas Mouthpiece assembly* with noseclip as follows: Tedlar flap valves cut to replace the rubber valves supplied, 2 sections of 1 1/4 in o.d. copper tubing with 90° elbow (see Figure B-3), all joints were soldered and the entire piece nickel-plated.
9. Spring or wire spiral (1) 3 cm diameter and 6-7 cm in length, chrome or nickel-plated. (This device keeps the intake end of Tedlar Bag A from collapsing during inhalations).
10. Teflon® tubing, 1/4-in o.d. 2-3 M.
11. Glass "Y", 1/4 in x 8 mm x 8 mm.
12. Teflon® straight union reducers (4) (Beckman, 830511).
13. Straight unions, stainless steel with Teflon® ferrules 1/4 in (5) [Swagelok: SS-400-6, T-404-1, T-403-1].
14. Glass or plastic tubing 8-mm i.d., 2 cm in length (2).
15. "Y" connector, polypropylene (1) [Fisher: 15-320-10D].
16. Forceps, 200 mm (2) [Fisher 10-316A].
17. Cast iron ring stand, 10 x 15 cm base (1).
18. Drying tubes, polyethylene, 152 mm (1 or more).
19. Rubber tubing 1/4-in i.d., 3/32-in wall thickness.
20. Quick Connect with Teflon® or nylon ferrules [open] (1) [Swagelok: brass or stainless steel - QC4-S-400].
21. Pump, Nutech Model 220 (Nutech Inc., Durham, NC) or equivalent (1).
22. Stopwatch (1).
23. Glovebag with clips [I^2R: x-24-17]; (Optional) Helium tank and regulator; Teflon® tubing to connect tank and glove bag; ring stand and clamp.
24. Binder clips, large (1 or more) to close ducts of Tedlar bags.
25. Drierite (>20% indicating) (500 g or more).

---

*Sargent Welch Cat. No. S-7695 (not currently in stock).

26. Helium tank and regulator with quick-connect body. Use activated charcoal filter in-line.

27. Stopper ties with paper clips (2) (Fisher, 14-632).

28. Distilled water.

29. Tenax cartridges and storage containers--1.6 x 10 cm glass tubes filled with 6 cm of 35/60 mesh Tenax held in place with glass wool plugs (see Appendix A for details).

30. Ethanol and swabs for sterilizing equipment.

PROCEDURE

Fill the humidifier with 100 mL distilled water. Evacuate both Tedlar bags using the pump with the mouthpiece plug in place. Place cleaned Tenax cartridges in their fittings between Tedlar Bag B and the pump.

The valve from the ultrapure air is opened and Bag A partially inflated with a plug in the mouthpiece. The subject is then attached to the apparatus with the nosepiece in place and allowed to breath, inhaling from Bag A and exhaling into Bag B. When Bag B is partially inflated, the pump is started at a nominal 7 L/min. The flow rate is then adjusted to approximate the subject's breathing rate. The test is continued until 60 L of breath have been collected or 15 min pass whichever occurs first. The subject is then removed from the apparatus and the plug replaced in the mouthpiece and Bag B is exhausted through the two parallel cartridges.

Data concerning the breath collection are recorded. Subject code number, time at start and end, pump meter readings beginning and end, and ambient temperature are all recorded to permit quantitation later.

See Appendix A for the Tenax cartridge analysis.

Reference

1. J. P. Conkle, B. J. Camp, and B. E. Welch, Trace Composition of Human Respiratory Gas, Arch Environ. Health, 30, 290-95 (1975).

APPENDIX C

SEQUENTIAL WITHOUT REPLACEMENT SAMPLING FOR ATTRIBUTES AND SUBPOPULATION MEANS

SEQUENTIAL WITHOUT REPLACEMENT SAMPLING FOR ATTRIBUTES AND SUBPOPULATION MEANS

Consider a finite population with N units u(i); i = 1(1)N. We will denote this universe by U = {u(i); i = 1(1)N}. This population contains some number M of units belonging to a particular subpopulation or domain of interest D, where M is unknown. Let $P_D = M/N$ denote the unknown population proportion belonging to domain D. If Y(i) denotes a variate value of interest associated with the i-th population member, then we define

$$Y_D(+) = \sum_{i \varepsilon D} Y(i) \tag{1}$$

and

$$Y_D(\cdot) = Y_D(+)/M \tag{2}$$

Now, we examine a without replacement sampling scheme analogous to the familiar with replacement method that leads to the negative binomal distribution. We state the following theorem:

Theorem 1. If units are selected with equal probabilities and without replacement from a finite universe of size N until m members of a particular domain D have been selected, then n (the number of draws required to yield m members of D) has the following distribution:

$$\Pr\{n = r/M\} = \frac{M}{N} \binom{M-1}{m-1} \binom{N-M}{r-m} \quad \binom{N-1}{r-1} \qquad \text{for } r = m, \ldots, N-M+m$$

which can also be written

$$\Pr\{n = r/P_D) = P_D \binom{NP_D-1}{m-1} \binom{NQ_D}{r-m} \binom{N-1}{r-1} \qquad \text{for } r = m, \ldots, N-M=M$$

where $Q_D = (1-P_D)$. Notice that P_D can take the values 0,(1/N), (2/N). . ., (K/N),. . .1. This distribution will be referred to as the Negative Hypergeometric distribution.

Proof. For m members of D to have been selected after the n-th draw requires that m-1 had been selected after the (n-1)-th, draw, the final member of D being selected on draw n. Therefore,

$$\Pr(n = r/M) = \left\{ \frac{\binom{M}{m-1}\binom{N-M}{r-m}}{\binom{N}{r-1}} \right\} x \left\{ \frac{M-m+1}{N-r+1} \right\}$$

Recall the factorial equation for combinations is of the form:

$${}_n C_r = \frac{n!}{(n-r)!r!}$$

and write

$$\Pr(n = r/m) = \frac{\left\{ \frac{M!}{(M-m+1)!(m-1)!} \quad \frac{(N-M)!}{(N-M-r+m)!(r-m)!} \quad \frac{M-m+1}{N-r+1} \right\}}{\frac{N!}{(N-r+1)!(r-1)!}}$$

$$= \frac{\frac{M! \; (M-m+1)}{(M-m+1)!(m-1)!} \cdot \binom{N-M}{r-m}}{\frac{N! \; (N-r+1)}{(N-r+1)!(r-1)!}}$$

$$= \frac{\frac{M!}{(M-m)!(m-1)!} \binom{N-M}{r-m}}{\frac{N!}{(N-r)!(r-1)!}}$$

$$= \frac{M \binom{M-1}{m-1} \binom{N-M}{r-m}}{N \binom{N-1}{r-1}}$$

which is the result stated in Theorem 1.

The following corollary is an immediate consequence of Theroem 1.

Corollary 1. If X = n-m is number of units in the sample of Theorem 1 that do not belong to D, then

$$\Pr(X = x) = P_D \binom{M-1}{m-1}\binom{N-M}{x} \Big/ \binom{N-1}{m+x-1}$$

for $x = 0,1,\ldots,N-M$

implying that

$$\sum_{x=0}^{N-M} \binom{N-M}{x} \Big/ \binom{N-1}{m+x-1} = P_D^{-1} \binom{M-1}{m-1}^{-1}$$

$$= \frac{N}{M} \left\{ \frac{(M-1)!}{(M-1-m+1)!\,(m-1)!} \right\}^{-1}$$

$$= \left(\frac{N}{M}\right)\left(\frac{M}{m}\right) \left\{ \frac{M!}{(M-m)!\,m!} \right\}^{-1}$$

$$= \frac{N}{m} \binom{M}{m}^{-1}$$

where M!, for example, is M factorial or M(M-1)(M-2). . . 1

Applying the results of Theorem 1 or more specifically, its corollary, we can show that (m-1)/(n-1) is an unbiased estimate of P_D. Notice, that

$$E\{(n-1)^{-1}\} = E\{(m+x-1)^{-1}\}$$

Now,

$$E\{(m+x-1)^{-1}\} = P_D \binom{M-1}{m-1} \sum_{x=0}^{N-M} \binom{N-M}{x} \Big/ (m+x-1) \binom{N-1}{m+x-1}$$

$$= \frac{P_D}{N-1} \binom{M-1}{m-1} \sum_{x=0}^{N-M} \binom{N-M}{x} \Big/ \binom{N-2}{m+x-2}$$

Letting $\mathit{N} = \mathrm{N}-1$, $\mathit{M} = \mathrm{M}-1$ and $\mathit{m} = \mathrm{m}-1$, we see from corollary 1 that the sum above is

$$\frac{\mathit{N}}{\mathit{m}} \binom{\mathit{M}}{\mathit{m}}^{-1} = \frac{\mathrm{N}-1}{\mathrm{m}-1} \binom{\mathrm{M}-1}{\mathrm{m}-1}^{-1}$$

where

$$\bar{y}_D(m-1) = \sum_{k=1}^{m-1} Y(k)/(m-1)$$

is the simple average of the variate values associated with the first (m-1) units drawn that belong to domain D. Notice, that if the m-th such unit is selected at the n-th draw, then the (m-1) units selected up to and including the (n-1)-th draw constitute a simple random sample from domain D of unknown size M. Therefore, given that the m-th member of D is selected on draw n, we have

$$E\{\bar{y}_D(m-1) \mid n\} = Y_D(\cdot)$$

and

$$\mathrm{Var}\{\bar{y}_D(m-1) \mid n\} = \left(\frac{1}{m-1} - \frac{1}{M}\right) S_D^2$$

Therefore,

$$E\{\hat{Y}_D(+) = N\hat{P}_D\ \bar{y}_D(m-1) \mid n=r\} = N\hat{P}_D\ Y_D(\cdot) \quad \text{and}$$

$$\mathrm{Var}\{\hat{Y}_D(+) \mid n=r\} = N^2\ \hat{P}_D^2 \left(\frac{1}{m-1} - \frac{1}{M}\right) S_D^2$$

Having shown that $\hat{P}_D$ is an unbiased estimate of P_D, it is clear that $\hat{Y}_D(+)$ is an unbiased estimator for $Y_D(+)$. The variance of $\hat{Y}_D(+)$ is

$$\mathrm{Var}\{\hat{Y}_D(+)\} = N^2\ Y_D^2(\cdot)\ \ \mathrm{Var}\{\hat{P}_D\} + N^2\left(\frac{1}{m-1} - \frac{1}{M}\right) S_D^2\ \ E\{\hat{P}_D^2\} \qquad (5)$$

The variance expression in (5) can be recast as follows:

$$\mathrm{Var}\{\hat{Y}_D(+)\} = N^2 \ \mathrm{Var}\{\hat{P}_D\} \left\{ \left(\frac{1}{m-1} - \frac{1}{M} \right) S_D^2 + Y_D^2(\cdot) \right\}$$

$$+ \ N^2 \ P_D^2 \left(\frac{1}{m-1} - \frac{1}{M} \right) S_D^2$$

Given that the m-th sample member from domain D is selected on the n-th draw, we see that

$$E\{\bar{y}_D^2(m-1) \mid n\} = \mathrm{Var}\{\bar{y}_D(m-1) \mid n\} + E^2\{\bar{y}_D(m-1) \mid n\}$$

$$= \left\{ \left(\frac{1}{m-1} - \frac{1}{M} \right) S^2{}_D + Y_D^2(\cdot) \right\}$$

Also, with

$$s_D^2(m-1) = \sum_{k=1}^{m-1} [Y(k) - \bar{y}_D(m-1)]^2/(m-2)$$

$$= SS_D(m-1)/(m-2)$$

denoting the standard mean square among the first (m-1) variates associated with domain D, we see that

$$E\{s_D^2(m-1) \mid n\} = S_D^2$$

This allows us to write

$$\mathrm{Var}\{\hat{Y}_D(+)\} = N^2 \left[E\{\mathrm{var}(\hat{P}_D)\} \ E\{\bar{y}_D^2(m-1) \mid n\} \right.$$

$$\left. + \left\{ \frac{P_D^2}{(m-1)} - \frac{P_D}{N} \right\} E\{s_D^2(m-1) \mid n\} \right]$$

Finally, noting that

$$\left\{ \frac{\widehat{(P_D^2)}}{(m-1)} - \frac{\hat{P}_D}{N} \right\} = \frac{(m-2)}{(n-1)(n-2)} \left[1 - \frac{(n-1)}{N} \right] ,$$

we see that

$$\mathrm{var}\{\hat{Y}_D(+)\} = N^2 \left\{ \mathrm{var}(\hat{P}_D)\ \bar{y}_D^2(m-1) + [1 - \frac{(n-1)}{N}]\ \frac{SS_D(m-1)}{(n-1)(n-2)} \right\}$$

Recalling that

$$\mathrm{var}(\hat{P}_D) = [1 - \frac{(n-1)}{N}]\ \frac{\hat{P}_D(1-\hat{P}_D)}{(n-2)} ,$$

we find that

$$\mathrm{var}\{\hat{Y}_D(+)\} = N^2\ [1 - \frac{(n-1)}{N}]\ \left\{ P_D(1-P_D)\ \bar{y}_D^2(m-1) + \frac{SS_D(m-1)}{(n-1)} \right\} \Big/ (n-2)$$

The quantity in curly brackets above can be expanded, noting that

$$SS_D(m-1)/(n-1) = \sum_{i=1}^{n-1} z^2(i)/(n-1) - \hat{P}_D\ \bar{y}_D^2(m-1)$$

where $z(i) = I_D(i)\ Y(i)$

with

$$I_D(i) = \begin{cases} 1 & \text{if } u(i) \varepsilon D \\ 0 & \text{otherwise} \end{cases} .$$

Letting

$$\bar{z}_D(n-1) = \sum_{i=1}^{n-1} z(i)/(n-1) = \hat{P}_D\ \bar{y}_D(m-1)$$

and define

$$s_z^2 = \sum_{i=1}^{n-1} [z(i) - \bar{z}_D(n-1)]^2/(n-2) ,$$

we can write $\mathrm{var}\{\hat{Y}_D(+)\}$ as

$$\mathrm{var}\{\hat{Y}_D(+) \quad = \quad N\ \bar{z}(n-1)\} \quad = \quad N^2\ [\ \frac{1}{(n-1)} - \frac{1}{N}\ ]\ \ s_z^2\ . \tag{6}$$

Again, we notice that the form of $\mathrm{var}\{\hat{Y}_D(+)\}$ is identical to the form of the unbiased variance estimator for a domain total when a simple random sample of fixed size (n-1) is drawn without replacement.

To extend these results to a stratified sequential scheme, we define

$$Y_D(h+) = \sum_{i\varepsilon D(h)} Y_D(hi)$$

as the population total for domain D in stratum $h = 1(1)H$. The corresponding stratum average is denoted by $Y_D(h\cdot) = Y_D(h+)/M(h)$. We are interested in estimating the population average

$$\bar{Y}_D \quad = \quad \sum_{h=1}^{H} Y_D(h+)\ /\ \sum_{h=1}^{H} M(h)$$

$$= \quad Y_D(++)\ /\ M(+)$$

for domain D. We propose the ratio estimator

$$\hat{\bar{Y}}_D \quad = \quad \sum_{h=1}^{H} N(h)\ \hat{P}_D(h)\ \bar{y}_D(h)\ /\ \sum_{h=1}^{H} N(h)\ \hat{P}_D(h) \tag{7}$$

where

$N(h)$ is the population size of stratum (h)

$\hat{P}_D(h)$ = $[m(h) - 1]/[n(h) - 1]$ is the stratum (h) estimate for $P_D(h) = M(h)/N(h)$ the proportion of domain D members in stratum (h).

$\bar{y}_D(h)$ is the simple average of the [m(h) - 1] variate values associated with the first [m(h) - 1] members of domain D(h) selected for the sample.

To estimate the variance of $\hat{\bar{\bar{Y}}}_D$ in (7), we will use the approximate variance formula for a ratio

$$
\begin{aligned}
\mathrm{Var}\{\hat{\bar{\bar{Y}}}_D &= \hat{Y}_D(++)/\hat{M}(+)\} \\
&\doteq \Big[\mathrm{Var}\{\hat{Y}_D(++)\} + \bar{Y}_D^2 \,\mathrm{Var}\{\hat{M}(+)\} \\
&\quad - 2\, \bar{Y}_D \,\mathrm{Cov}\{\hat{Y}_D(++);\, \hat{M}(+)\}\Big] \Big/ M^2(+)
\end{aligned}
$$

to suggest the estimator

$$
\begin{aligned}
\mathrm{var}\{\hat{\bar{\bar{Y}}}_D\} &= \Big[\mathrm{var}\{\hat{Y}_D(++)\} + \hat{\bar{\bar{Y}}}_D^2 \,\mathrm{var}\{\hat{M}(+)\} \\
&\quad - 2\, \bar{\bar{Y}}_D^2 \,\mathrm{cov}\{\hat{Y}_D(++);\, \hat{M}(+)\}\Big] \Big/ \hat{M}^2(+) \,. \qquad (8)
\end{aligned}
$$

The covariance between

$$\hat{Y}_D(++) = \sum_{h=1}^{H} N(h)\, \hat{P}_D(h)\, \bar{y}_D(h)$$

and

$$\hat{M}(+) = \sum_{h=1}^{H} N(h)\, \hat{P}_D(h)$$

can be written as

$$\mathrm{Cov}\{\hat{Y}_D(++);\, \hat{M}(+)\} = \sum_{h=1}^{H} N^2(h)\, \mathrm{Cov}\{\hat{P}_D(h)\bar{y}_D(h);\, \hat{P}_D(h)\}$$

where

$$\mathrm{Cov}\{\hat{P}_D(h)\bar{y}_D(h);\, \hat{P}_D(h)\} = \bar{Y}_D(h)\, \mathrm{Var}\{\hat{P}_D(h)\} \qquad (9)$$

where $\bar{Y}_D(h) = Y_D(h+)/M(h)$ is the domain D(h) average. The obvious estimator for the covariance expression in (9) is

$$\text{cov}\{\hat{P}_D(h)\bar{y}_D(h);\ \hat{P}_D(h)\} \ = \ \bar{y}_D(h)\ \text{var}\{\hat{P}_D(h)\} \quad . \tag{10}$$

Using the covariance estimator in (10), we can expand the variance estimator in (8) to

$$\begin{aligned}\text{var}\{\hat{\bar{Y}}_D\} \ = \ \sum_{h=1}^{H} N^2(h) \Big\{&\text{var}[\hat{P}_D(h)\bar{y}_D(h)] + \hat{\bar{Y}}_D^2\ \text{var}[\hat{P}_D(h)] \\ &- 2\ \hat{\bar{Y}}_D\ \text{cov}[\hat{P}_D(h)\bar{y}_D(h);\ \hat{P}_D(h)]\Big\} \Big/ \hat{M}^2(+) \quad .\end{aligned}$$

Defining

$$I_D(hi) \ = \ \begin{cases} 1 & \text{if sampling unit } u(hi) \ \varepsilon \ D(h) \\ 0 & \text{otherwise} \end{cases}$$

and let

$$z_D(hi) \ = \ I_D(hi)\ Y(hi)$$

then, we have shown that

$$\begin{aligned}\bar{z}_D(h) \ &= \ \sum_{i=1}^{n(h)-1} z_D(hi) \ / \ [n(h) - 1] \\ &= \ \hat{P}_D(h)\bar{y}_D(h)\end{aligned}$$

and

$$s_z^2(h) \ = \ \sum_{i=1}^{n(h)-1} [z_D(hi) - \bar{z}_D(h)]^2 \ / \ [n(h) - 2]$$

can be used to calculate

$$\mathrm{var}\{\hat{P}_D(h)\bar{y}_D(h)\} = \left[\frac{1}{n(h)-1} - \frac{1}{N(h)}\right] s_z^2(h) \quad .$$

It is also clear that

$$I_D(h\cdot) = \hat{P}_D(h)$$

and

$$s_I^2(h) = \sum_{i=1}^{n(h)-1} [I_D(hi) - I_D(h\cdot)]^2 \,/\, [n(h) - 2]$$

$$= \left[\frac{n(h)-1}{n(h)-2}\right] \hat{P}_D(h)\,[1 - \hat{P}_D(h)]$$

leading to

$$\mathrm{var}\{\hat{P}_D(h)\} = \left[\frac{1}{n(h)-1} - \frac{1}{N(h)}\right] s_I^2(h)$$

$$= \left[1 - \frac{n(h)-1}{N(h)}\right] \hat{P}_D(h)\,[1 - \hat{P}_D(h)] \quad .$$

It is also possible to show that

$$\mathrm{cov}\{\hat{P}_D(h)\bar{y}_D(h);\ \hat{P}_D(h)\} = \left[\frac{1}{n(h)-1} - \frac{1}{N(h)}\right] s_{zI}$$

where

$$s_{zI} = \sum_{i=1}^{n(h)-1} [z_D(hi) - \bar{z}_D(h)]\,[I_D(hi) - I_D(h\cdot)] \,/\, [n(h) - 2]$$

$$= \bar{y}_D(h) \left[\frac{n(h)-1}{n(h)-2}\right] \hat{P}_D(h)\,[1 - \hat{P}_D(h)] \quad .$$

Finally, we have shown that

$$\operatorname{var}\{\hat{\bar{\bar{Y}}}_D\} = \sum_{h=1}^{H} N^2(h) \left[\frac{1}{n(h)-1} - \frac{1}{N(h)}\right] \left[s_z^2(h) + \hat{\bar{\bar{Y}}}{}_D^2 \, s_I^2(h) - 2 \, \hat{\bar{\bar{Y}}}_D \, s_{zI}(h) \right] \Big/ \hat{M}^2(+) \quad .$$

If we let

$$t_D(hi) = N(h) \, I_D(hi) \, [Y(hi) - \hat{\bar{\bar{Y}}}_D] \, / \, \hat{M}(+)$$

or

$$t_D(hi) = W(h) \, I_D(hi) \, [Y(hi) - \hat{\bar{\bar{Y}}}_D] \, / \, \hat{P}_D$$

where

$$W(h) = N(h)/N(+)$$

$$\hat{P}_D = \hat{M}(+)/N(+)$$

then

$$\operatorname{var}\{\hat{\bar{\bar{Y}}}_D\} = \sum_{h=1}^{H} \left\{ \frac{1}{[n(h)-1]} - \frac{1}{N(h)} \right\} s_t^2(h) \quad . \tag{11}$$

If [n(h) - 1] << N(h) for all h = 1(1)H, then equation (11) is approximately

$$\operatorname{var}\{\hat{\bar{\bar{Y}}}_D\} \doteq \sum_{h=1}^{H} s_t^2(h)/[n(h) - 1] \quad . \tag{12}$$

It is intriguing to notice that by discarding the n(h)-th unit in the sequential draw from stratum (h) we can treate the previous [n(h) - 1] units as a simple random sample of fixed size drawn without replacement. Faced with the results outlined in the previous paragraphs, one would be tempted to conjecture that given the value of n(h), these n(h) - 1 observations are, in fact, equivalent to a SRS of fixed size. This contention can be easily disproved by using the 'Negative-Hypergeometric' distribution for n(h) in Theorem 1 to show for a particular example (say N = 5, M = 3 and m =2) that

$$\mathrm{Var}\left\{\left(\frac{m-1}{n-1}\right) = \hat{P}_D\right\} \neq \left[E\left(\frac{1}{n-1}\right) - \frac{1}{N}\right]\left(\frac{N}{N-1}\right) \quad P_D(1 - P_D)$$

$$= \left[\frac{P_D}{(m-1)} - \frac{1}{N}\right]\left(\frac{N}{N-1}\right) \quad P_D(1 - P_D)$$

$$= \frac{(M-m+1)\ M(N-M)}{(m-1)\ N^2\ (N-1)} \ .$$

Or

$$E\left\{\frac{(m-1)^2}{(n-1)^2}\right\} \neq \left(\frac{M}{N}\right)^2 \left[\frac{(M-m+1)\ (N-M)}{(m-1)\ M(N-1)} + 1\right] \ . \qquad (13)$$

For the example mentioned above with N = 5, M = 3, m = 2

$$E\left\{\frac{(m-1)^2}{(n-1)^2}\right\} = (m-1)^2 \quad E\ \{(m+x-1)^{-2}\}$$

$$= (m-1)^2\ P_D \cdot \binom{M-1}{m-1} \sum_{x=0}^{N-M} \binom{N-M}{x} \Big/ (m+x-1)^2 \binom{N-1}{m+x-1}$$

$$= \left(\frac{3}{5}\right)\ 2 \sum_{x=0}^{2} \binom{2}{x} \Big/ (x+1)^2 \binom{4}{x+1}$$

$$= \left(\frac{6}{5}\right) \left\{1/4 + 2/4\mathrm{x}6 + 1/9\mathrm{x}4\right\}$$

$$= \frac{6}{5\text{x}4} \left\{ 1 + 1/3 + 1/9 \right\}$$

$$E\{\hat{P}_D^2\} = \frac{6 \times 13}{5 \times 4 \times 9} = 13/30 \quad .$$

The right-hand side of (13) is

$$\left(\frac{3}{5}\right)^2 \left[\frac{2 \times 2}{3 \times 4} + 1\right] = \frac{12}{25} \neq E\{\hat{P}_D^2\} \quad .$$

This small counter-example is sufficient to show that the first n(h)-1 units do not constitute a SRS of fixed size conditional on n(h). This is one example (counter-example) used to demonstrate that the technique of n associated with m+1 is needed to obtain unbiased estimates for the m values obtained from this selection process.

APPENDIX D

DATA COLLECTION INSTRUMENTS FOR THE HOUSEHOLD SURVEY AND MATERIAL SUBMITTED TO OMB

OMB No. 158-S78010
Approval Expires September 1980

RESEARCH TRIANGLE INSTITUTE
STUDY OF BENZENE BODY-BURDEN

PARTICIPANT CONSENT FORM
(HIGH EXPOSURE AREA)

I understand that the Research Triangle Institute is engaged in a study of the exposure and absorption of benzene by persons living in areas having various levels of benzene in the environment. I understand that the survey is being conducted in order to help measure the levels of exposure and absorption of benzene in populations environmentally exposed to benzene, and is limited to the purpose stated. I further understand that the survey is being conducted under the auspices of the United States Environmental Protection Agency in cooperation with the

Texas and City of Houston Health Departments.

I do hereby freely consent to participate in this study of benzene exposure and absorption and understand that my participation will consist of providing answers to a questionnaire related to environmental exposure and the following environmental and biological samples: (1) two four ounce samples of cold tap water from a source commonly used for drinking and cooking, (2) a sample of environmental exposure collected by a small device which I will keep with me for a short time, (3) a small (approximately 10 cc) blood sample to be taken from an arm vein, and (4) a breath sample. I understand that an agent of the Research Triangle Institute will administer the questionnaire in my home and at the same time collect the tap water samples, instruct me regarding the exposure monitoring device, and make arrangements regarding collection of the breath and blood samples. I understand that after the collection of the breath and blood samples I will receive an incentive of ten dollars for my full participation in the study. I understand that a small number of households and individuals will be selected for the collection of duplicate tap water and blood samples and reinterview, but that such selection would not entitle me to further compensation.

I understand that my name will not be voluntarily disclosed, and that my name will not be referred to in any way when compiling and evaluating the results of the study. I understand that participation in this study may result in no direct benefits to me, other than those described herein, and that I am free to withdraw from this study at any time. It has been explained to me that there are no significant risks to me from participation in this study. I further understand that while participating in the study I will be free to ask any questions concerning the study; if I have any further questions about the project, I know that I am free to contact

Dr. Richard K. Donelson, Texas Department of Health telephone number 512-458-7328 or

Dr. Robert A. MacLean, City of Houston Health Dept. telephone number 713-222-4295

or Mr. Benjamin S. H. Harris, III, Survey Operations Center, Research Triangle Institute, Research Triangle Park, North Carolina 27709, telephone number 919-541-6055.

Date: ☐☐ - ☐☐ - ☐☐
(Month) (Day) (Year)

Participant's Name: ____________________
(Print)

Site Number: ☐ Segment Number: ☐☐ Household Number: ☐☐☐ Participant Number: ☐☐

SIGNATURES:

Participant: ____________________ Witness: ____________________

Interviewer Number: ☐☐☐

OMB No. 158-S78010
Approval Expires September 1980

RESEARCH TRIANGLE INSTITUTE

STUDY OF BENZENE BODY-BURDEN

NOTICE: The information recorded on this questionnaire will be held in strict confidence, and will be used solely for research into the effects of environmental factors on public health. All results will be summarized for groups of people; no information about individual persons will be released without the consent of the individual. This questionnaire is authorized by law (P.L.94-469). While you are not required to respond, your cooperation is needed to make the results of the survey comprehensive, accurate, and timely.

HOUSEHOLD SCREENING QUESTIONNAIRE

1. Site number: ☐   2. Segment number: ☐☐   3. Household/housing unit number: ☐☐☐

4. Interviewer number: ☐☐☐   5. Date: ☐☐ - ☐☐ - ☐☐ *(Month)* *(Day)* *(Year)*

6. a. What is the exact address of this housing unit?

____
(Street Number and Name) *(Apartment Number)*

______________________________ ☐☐☐☐☐
(City) *(State)* *(Zip Code)*

b. Is this an eligible housing unit? ☐1 Yes *(Go to Question 7)* ☐2 No *(Go to Question 6c)*

c. If no, indicate reason and STOP! ☐1 Vacant ☐2 Nonexistent ☐3 Business ☐4 Group quarters ☐5 Vacation quarters ☐6 Other *(Specify)* ______________

7. a. Do you have a responsible screening respondent? ☐1 Yes *(Go to Question 7b)* ☐2 No *(Go to Question 7c)*

b. If yes, indicate whether respondent is ☐1 Household respondent ☐2 Neighbor respondent

c. If no, indicate reason and STOP! ☐1 Refusal ☐2 No response after ☐ calls ☐3 Other *(Specify)* ______________

---

8. a. Do you have a telephone? ☐1 Yes *(Go to Question 8b)* ☐2 No *(Go to Question 8c)*

b. If yes, what is the number? ☐1 Unlisted ☐2 Refused ☐☐☐ - ☐☐☐ - ☐☐☐☐ *(Area Code)* *(Go to Question 9)*

c. If no, what is the number of the nearest telephone? ☐☐☐ - ☐☐☐ - ☐☐☐☐ *(Area Code)* ☐1 Do not know

9. How many persons reside in this household? ☐☐

10. For each person in your household, including yourself, please indicate:

- a. Age *(in years as of last birthday)*,
- b. Sex *(M for male, F for female)*,
- c. Whether or not each person is a smoker *(1 = Yes, 2 = No, 3 = Do not know)*,
- d. Whether or not each person presently suffers respiratory distress *(1 = Yes, 2 = No, 3 = Do not know)*,
- e. Whether or not each person is presently under medical care *(1 = Yes, 2 = No, 3 = Do not know)*,
- f. Whether or not each person is presently taking prescription medication *(1 = Yes, 2 = No, 3 = Do not know)*,
- g. Each person's primary hobby *(such as stamps, coins, painting, gardening, building models, refinishing furniture, etc.)*,
- h. The nature of the business where each person works *(such as at home, school, service station, bank, etc.)*, and
- i. Relationship to you,

beginning with the oldest and proceeding to the youngest *(Enter appropriate codes or responses in matrix below)*:

Household Member Number	a. Age (Years)	b. Sex (M or F)	c. Smoker	d. Respiratory Distress	e. Medical Care	f. Prescription Medication	g. Hobby	h. Nature of Business	i. Relationship to Respondent	Participant Number	
01											
02											
03											
04											
05											
06											
07											
08											
09											
10											

11. a. Does anyone in your household have as a hobby painting, building models, gardening, or refinishing furniture?

☐1 Yes *(Go to Question 11b)* ☐2 No ☐3 Do not know *(Go to Question 12)*

b. If yes, indicate relationship to respondent ______________________________

and household member number(s) from Question 10 ______________

12. a. Is anyone in your household employed as a painter or in a service station, garage, furniture repair shop, or chemical plant?

☐1 Yes *(Go to Question 12b)* ☐2 No ☐3 Do not know *(Go to Question 13)*

b. If yes, indicate relationship to respondent ______________________________

and household member number(s) from Question 10 ______________

13. Is anyone in the household eligible to participate in the survey? ☐1 Yes *(Go to Question 14)* ☐2 No *(STOP!)*

If it is apparent that the household contains no persons eligible to participate in this study, thank the respondent and proceed to the next household. However, if persons in the household appear to be eligible to participate in this study, continue to question 14.

14. Would you participate in a health study as a paid volunteer? ☐1 Yes ☐2 No ☐3 Do not know ☐4 Ineligible

15. In your opinion, would other members of your household participate in a health survey as a paid volunteer?

☐1 Yes, all ☐2 Yes, some ☐3 No ☐4 Do not know ☐5 Ineligible

RESEARCH TRIANGLE INSTITUTE

STUDY OF BENZENE BODY-BURDEN

HOUSEHOLD SCREENING LOG

Site Number ☐ Segment Number ☐☐ Interviewer Number ☐☐☐

Date ☐☐ – ☐☐ – ☐☐ Day of Week ☐
(Month) (Day) (Year)

Household/ Housing Unit Number			Street Address or Description	Eligible Household Member(s)		Member(s) Agree(s) to Participate		Number of Participants		Reason(s) for Nonparticipation, Nonresponse, or Ineligibility
				Yes	No	Yes	No			

COMMENTS

OMB No. 158-S78010
Approval Expires September 1980

STUDY OF BENZENE BODY-BURDEN

Sponsored by:
Office of Toxic Substances
Environmental Protection Agency
Washington, D.C. 20460

Conducted by:
Research Triangle Institute
P.O. Box 12194
Research Triangle Park, North Carolina 27709

QUESTIONNAIRE

THE RESEARCH TRIANGLE INSTITUTE OF RESEARCH TRIANGLE PARK, NORTH CAROLINA, IS UNDERTAKING A RESEARCH STUDY FOR THE U.S. ENVIRONMENTAL PROTECTION AGENCY OF LEVELS OF BENZENE ABSORPTION BY PERSONS LIVING IN COMMUNITIES EXPOSED TO BENZENE. THE INFORMATION RECORDED IN THIS QUESTIONNAIRE WILL BE HELD IN STRICT CONFIDENCE AND WILL BE USED SOLELY FOR RESEARCH INTO THE EFFECTS OF ENVIRONMENTAL FACTORS ON PUBLIC HEALTH. ALL RESULTS WILL BE SUMMARIZED FOR GROUPS OF PEOPLE; NO INFORMATION ABOUT INDIVIDUAL PERSONS WILL BE RELEASED WITHOUT THE CONSENT OF THE INDIVIDUAL. THIS QUESTIONNAIRE IS AUTHORIZED BY LAW (P.L. 94-469). WHILE YOU ARE NOT REQUIRED TO RESPOND, YOUR COOPERATION IS NEEDED TO MAKE THE RESULTS OF THIS SURVEY COMPREHENSIVE, ACCURATE, AND TIMELY.

Study number: ☐☐☐☐☐☐

Site number: ☐ Segment number: ☐☐ Household number: ☐☐☐ Participant number: ☐☐

NOTES

First, I would like to ask some general questions about you.

1. Sex *(by observation)*: ☐1 Male ☐2 Female

2. Race:
   - ☐1 Hispanic
   - ☐2 American Indian/Alaskan Native
   - ☐3 Black, not of Hispanic origin
   - ☐4 Asian/Pacific Islander
   - ☐5 White, not of Hispanic origin
   - ☐6 Other *(Specify)* ________

3. Household member number *(from HSQ)*: ☐☐

4. What was your age in years at last birthday? ☐☐ Years

5. What is your birthdate?

   (Month) ☐☐ – *(Day)* ☐☐ – *(Year)* ☐☐

6. What is your approximate weight in pounds?

   ☐☐☐ lbs. ☐1 Do not know

7. What is your approximate height in feet and inches?

   ☐ Feet ☐☐ Inches

Next, I would like to ask some questions about your occupation.

8. Are you presently employed in any capacity? ☐1 Yes *(Continue)* ☐2 No *(Go to Q. 12)*

9. How long have you been employed by your present employer? ☐☐ Units ☐1 Days ☐2 Months ☐3 Years

10. Does your occupation usually take you away from home? ☐1 Yes *(Continue)* ☐2 No *(Go to Q. 13)*

11. What is the nature and location (street address) of the company for which you work?

    (Specify) ________________________ ☐☐☐☐☐ *(Zip Code)*

12. If not presently employed, which of the following best describes your status?

    ☐1 Housewife
    ☐2 Student
    } *(Go to Q. 16)*

    ☐3 Unemployed
    ☐4 Retired
    ☐5 Disabled
    } *(Continue)*

13. What is/was your usual occupation? *(Specify)* ________________________

14. Are you presently employed in this occupation? ☐1 Yes ☐2 No

15. If yes to above question, how long have you been employed in that occupation?

    (Questions 14 and 15 may be skipped for unemployed, retired, and disabled persons.) ☐☐ Units ☐1 Days ☐2 Months ☐3 Years

16. Have you worked at any of the following occupations/businesses at any time during the past week?

a.	Painting	☐1 Yes (STOP!)	☐2 No *(Continue)*
b.	Service station or garage	☐1 Yes (STOP!)	☐2 No *(Continue)*
c.	Chemical plant	☐1 Yes (STOP!)	☐2 No *(Continue)*
d.	Petroleum plant	☐1 Yes (STOP!)	☐2 No *(Continue)*
e.	Furniture refinishing or repair	☐1 Yes (STOP!)	☐2 No *(Continue)*

Next, I would like to ask some questions regarding your health and personal habits.

17. Do you smoke? ☐ 1 Yes (STOP!) ☐ 2 No *(Continue)*

18. What is the average number of hours that you spend out of doors each day? ☐☐ Hours

19. How many hours of the day, on the average, do you normally spend away from home?

Weekdays ☐☐ Hours Weekends ☐☐ Hours

20. What do you consider the current status of your health?

☐ 1 Excellent ☐ 2 Good ☐ 3 Fair ☐ 4 Poor

21. Are you currently taking any prescription medication(s) on a regular daily basis? ☐ 1 Yes (STOP!) ☐ 2 No *(Continue)*

22. Have you taken any non-prescription medications in the past 48 hours? ☐ 1 Yes ☐ 2 No

If yes, specify ______________________________

23. Are you presently under a doctor's care? ☐ 1 Yes ☐ 2 No

If yes, specify reason ______________________________

24. Are you presently suffering from any respiratory problems *(such as cold, cough, sore throat, flu, asthma, bronchitis, shortness of breath, laryngitis, pleurisy, etc.)?*

☐ 1 Yes (STOP!) ☐ 2 No *(Continue)*

25. Have you ever been treated for anemia? ☐ 1 Yes ☐ 2 No

26. How many eggs have you eaten in the past 48 hours? ☐☐

27. Do you pursue any of the following hobbies? *(Check all that apply.)*

☐ 1 Furniture refinishing
☐ 2 Painting
☐ 3 Scale models
☐ 4 Gardening

(If a positive response is obtained for any one of these, STOP!)

Lastly, I would like to ask some questions about your residence and household.

28. How many years have you lived in this area? ☐☐ Years

29. How long have you lived at this address? ☐☐ Units ☐ 1 Days ☐ 2 Months ☐ 3 Years

30. Do you cool your home with any of the following appliances? *(Check all that apply.)*

☐ 1 Central air conditioning
☐ 2 Window air conditioner(s)
☐ 3 Evaporative cooler(s)
☐ 4 Window fan(s)
☐ 5 Ceiling exhaust fan(s)
☐ 6 Circulating fan(s)
☐ 7 None of these
☐ 8 Do not know
☐ 9 Other *(Specify)* ______________

31. Does your household grow any of its own food in a home garden? ☐ 1 Yes ☐ 2 No ☐ 3 Do not know

If yes, specify location of garden ______________________________

32. Where does your household obtain fresh fruit and/or vegetables? *(Specify)* ______________

33. What is the primary source of your water for drinking?

☐ 1 Bottled water
☐ 2 Tap - municipal supply
☐ 3 Tap - community well
☐ 4 Tap - private well
☐ 5 Tap - cistern
☐ 6 Do not know
☐ 7 Other *(Specify)* ______________

34. Is that the same primary source of water for drink mixes such as coffee, tea, Kool-Aid, etc?

☐ 1 Yes ☐ 2 No *If no, how does it differ? (Specify)* ____________________

35. What is the primary source of your water for cooking?

☐ 1 Bottled water ☐ 3 Tap - community well ☐ 5 Tap - cistern

☐ 2 Tap - municipal supply ☐ 4 Tap - private well ☐ 6 Do not know

☐ 7 Other *(Specify)* ____________________

36. Does anyone else in your household smoke? ☐ 1 Yes ☐ 2 No ☐ 3 Do not know

If yes, check all that apply: ☐ 1 Cigarettes ☐ 2 Cigars ☐ 3 Pipe ☐ 4 Other *(Specify)* ____________________

37. Does anyone else in your household work at any of the following occupations/businesses? *(Check all that apply.)*

☐ 1 Painting ☐ 2 Service station/garage/engine repair ☐ 3 Chemical/petroleum plant ☐ 4 Furniture refinishing/repair

38. Does anyone else in your household pursue any of the following hobbies? *(Check all that apply.)*

☐ 1 Painting ☐ 2 Furniture refinishing ☐ 3 Scale models ☐ 4 Gardening

39. Has anyone else in your household ever been treated for anemia? ☐ 1 Yes ☐ 2 No ☐ 3 Do not know

If yes, specify household member number(s) from HSQ: ____________________

40. Has anyone in your household, including yourself, ever been treated for leukemia?

☐ 1 Yes ☐ 2 No ☐ 3 Do not know

If yes, specify household member number(s) from HSQ: ____________________

RESPONDENT/INTERVIEWER INFORMATION

41. Respondent: ☐ 1 Participant ☐ 2 Other *(Specify)* ____________________ Household member number (from HSQ): ☐☐

42. Interviewer number: ☐☐☐

43. Date of interview: ☐☐ *(Month)* – ☐☐ *(Day)* – ☐☐ *(Year)*

SAMPLE INFORMATION

44. Personnel monitor number ☐

	Date			Time	Flow Rate	Interviewer
	Month	Day	Year	Hours : Minutes	(ml/min)	Number
On				:		
Off				:		

COMMENTS: ____________________

45. Breath sample

Collected		Data on Collected Sample							
		Date			Time		Temp. C F	Volume Meter Reading (cubic feet)	Interviewer Number
					Start	Stop			
Yes	No	Month	Day	Year	Hours : Minutes	Hours : Minutes			
1	2				:	:			
	If not collected, reason:								

Apparatus number ☐

46. Tap water sample

Original Sample(s)						Interviewer Number	Duplicate Sample				
Collected		If Collected, Date			If Not Collected, Reason		Selected		Collected		If Not Collected, Reason
Yes	No	Month	Day	Year			Yes	No	Yes	No	
1	2						1	2	1	2	

Source: ____________________

47. Blood sample *(for high exposure area participants only).*

Original Sample						Interviewer Number	Duplicate Sample							
Collected		If Collected, Date			If Not Collected, Reason		Selected		Collected		If Collected, Date			If Not Collected, Reason
Yes	No	Month	Day	Year			Yes	No	Yes	No	Month	Day	Year	
1	2						1	2	1	2				

COMMENTS

OMB No. 158-S78010
Approval Expires September 1980

RESEARCH TRIANGLE INSTITUTE
STUDY OF BENZENE BODY-BURDEN

PARTICIPANT CONSENT FORM

I understand that the Research Triangle Institute is engaged in a study of the exposure and absorption of benzene by persons living in areas having various levels of benzene in the environment. I understand that the survey is being conducted in order to help measure the levels of exposure and absorption of benzene in populations environmentally exposed to benzene, and is limited to the purpose stated. I further understand that the survey is being conducted under the auspices of the United States Environmental Protection Agency in cooperation with the

Texas and City of Houston Health Departments.

I do hereby freely consent to participate in this study of benzene exposure and absorption and understand that my participation will consist of providing answers to a questionnaire related to environmental exposure and the following environmental and biological samples: (1) two four ounce samples of cold tap water from a source commonly used for drinking and cooking, (2) a sample of environmental exposure collected by a small device which I will keep with me for a short time, and (3) a breath sample. I understand that an agent of the Research Triangle Institute will administer the questionnaire in my home and at the same time collect the tap water samples, instruct me regarding the exposure monitoring device, and make arrangements regarding collection of the breath sample. I understand that after the collection of the breath sample I will receive an incentive of five dollars for my full participation in the study. I understand that a small number of households and individuals will be selected for the collection of duplicate tap water samples and reinterview, but that such selection would not entitle me to further compensation.

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Dr. Robert A. MacLean, City of Houston Health Dept. telephone number 713-222-4295

or Mr. Benjamin S. H. Harris, III, Survey Operations Center, Research Triangle Institute, Research Triangle Park, North Carolina 27709, telephone number 919-541-6055.

Date: ☐☐ - ☐☐ - ☐☐ (Month) (Day) (Year) Participant's Name: ______________________ (Print)

Site Number: ☐ Segment Number: ☐☐ Household Number: ☐☐☐ Participant Number: ☐☐

SIGNATURES:
Participant: ______________________ Witness: ______________________

Interviewer Number: ☐☐☐

OMB No. 158-S73010
Approval Expires September 1980

RESEARCH TRIANGLE INSTITUTE
STUDY OF BENZENE BODY-BURDEN

PARTICIPANT CONSENT FORM

(HIGH EXPOSURE AREA)

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Illinois Department of Public Health.

I do hereby freely consent to participate in this study of benzene exposure and absorption and understand that my participation will consist of providing answers to a questionnaire related to environmental exposure and the following environmental and biological samples: (1) two four ounce samples of cold tap water from a source commonly used for drinking and cooking, (2) a sample of environmental exposure collected by a small device which I will keep with me for a short time, (3) a small (approximately 10 cc) blood sample to be taken from an arm vein, and (4) a breath sample. I understand that an agent of the Research Triangle Institute will administer the questionnaire in my home and at the same time collect the tap water samples, instruct me regarding the exposure monitoring device, and make arrangements regarding collection of the breath and blood samples. I understand that after the collection of the breath and blood samples I will receive an incentive of ten dollars for my full participation in the study. I understand that a small number of households and individuals will be selected for the collection of duplicate tap water and blood samples and reinterview, but that such selection would not entitle me to further compensation.

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Robert L. Wheatley telephone number 217-782-4674 or

Genelle Moore telephone number 618-288-5756

or Mr. Harvey S. Zelon, Survey Operations Center, Research Triangle Institute, Research Triangle Park, North Carolina 27709, telephone number 919-541-6054.

Date: ☐☐ - ☐☐ - ☐☐ (Month) (Day) (Year)   Participant's Name: ____________ (Print)

Site Number: ☐   Segment Number: ☐☐   Household Number: ☐☐☐   Participant Number: ☐☐

SIGNATURES:

Participant: ____________   Witness: ____________

Interviewer Number: ☐☐☐

Medium
St. Louis

OMB No. 158-S78010
Approval Expires September 1980

RESEARCH TRIANGLE INSTITUTE
STUDY OF BENZENE BODY-BURDEN

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Missouri Department of Natural Resources and St. Louis Air Pollution Control.

I do hereby freely consent to participate in this study of benzene exposure and absorption and understand that my participation will consist of providing answers to a questionnaire related to environmental exposure and the following environmental and biological samples: (1) two four ounce samples of cold tap water from a source commonly used for drinking and cooking, (2) a sample of environmental exposure collected by a small device which I will keep with me for a short time, and (3) a breath sample. I understand that an agent of the Research Triangle Institute will administer the questionnaire in my home and at the same time collect the tap water samples, instruct me regarding the exposure monitoring device, and make arrangements regarding collection of the breath sample. I understand that after the collection of the breath sample I will receive an incentive of five dollars for my full participation in the study. I understand that a small number of households and individuals will be selected for the collection of duplicate tap water samples and reinterview, but that such selection would not entitle me to further compensation.

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Rick L. Roberts, Missouri Dept. of Nat. Resources telephone number 314-751-3241 or

Charles M. Copley or W. L. Hagar, St. Louis telephone number 314-622-3334

or Mr. Harvey S. Zelon, Survey Operations Center, Research Triangle Institute, Research Triangle Park, North Carolina 27709, telephone number 919-541-6054.

Date: ☐☐ - ☐☐ - ☐☐ (Month) (Day) (Year)

Participant's Name: ____________________ (Print)

Site Number: ☐ Segment Number: ☐☐ Household Number: ☐☐☐ Participant Number: ☐☐

SIGNATURES:

Participant: ____________________ Witness: ____________________

Interviewer Number: ☐☐☐

Low
St. Louis County

OMB No. 158-S78010
Approval Expires September 1980

RESEARCH TRIANGLE INSTITUTE
STUDY OF BENZENE BODY-BURDEN

PARTICIPANT CONSENT FORM

I understand that the Research Triangle Institute is engaged in a study of the exposure and absorption of benzene by persons living in areas having various levels of benzene in the environment. I understand that the survey is being conducted in order to help measure the levels of exposure and absorption of benzene in populations environmentally exposed to benzene, and is limited to the purpose stated. I further understand that the survey is being conducted under the auspices of the United States Environmental Protection Agency in cooperation with the

Missouri Department of Natural Resources and the St. Louis County Health Department.

I do hereby freely consent to participate in this study of benzene exposure and absorption and understand that my participation will consist of providing answers to a questionnaire related to environmental exposure and the following environmental and biological samples: (1) two four ounce samples of cold tap water from a source commonly used for drinking and cooking, (2) a sample of environmental exposure collected by a small device which I will keep with me for a short time, and (3) a breath sample. I understand that an agent of the Research Triangle Institute will administer the questionnaire in my home and at the same time collect the tap water samples, instruct me regarding the exposure monitoring device, and make arrangements regarding collection of the breath sample. I understand that after the collection of the breath sample I will receive an incentive of five dollars for my full participation in the study. I understand that a small number of households and individuals will be selected for the collection of duplicate tap water samples and reinterview, but that such selection would not entitle me to further compensation.

I understand that my name will not be voluntarily disclosed, and that my name will not be referred to in any way when compiling and evaluating the results of the study. I understand that participation in this study may result in no direct benefits to me, other than those described herein, and that I am free to withdraw from this study at any time. It has been explained to me that there are no significant risks to me from participation in this study. I further understand that while participating in the study I will be free to ask any questions concerning the study; if I have any further questions about the project, I know that I am free to contact

Rick L. Roberts, Missouri Dept. of Nat. Resources telephone number 314-751-3241 or

Clifford Mitchell, St. Louis County Health Dept. telephone number 314-726-1100

or Mr. Harvey S. Zelon, Survey Operations Center, Research Triangle Institute, Research Triangle Park, North Carolina 27709, telephone number 919-541-6054.

Date: ☐☐ - ☐☐ - ☐☐ (Month) (Day) (Year) Participant's Name: ____________________ (Print)

Site Number: ☐ Segment Number: ☐☐ Household Number: ☐☐☐ Participant Number: ☐☐

SIGNATURES:
Participant: ____________________ Witness: ____________________

Interviewer Number: ☐☐☐

MATERIAL SUBMITTED TO OMB WITH THE DATA COLLECTION INSTRUMENTS

1. Justification

Benzene is not only one of the most fundamental and well-known organic chemicals, but is also of major industrial importance. In the United States, benzene ranks 13th in volume (1) with a projected production for 1976 of 1.5 x 10^9 gallons (2). Approximately 88 percent of the domestic benzene production is from petroleum sources with the remainder from coal (3). The largest benzene source is from catalytic reforming processes at oil refineries. Other major production routes are dealkylation of toluene and as a co-product with ethylene from steam crackers (2).

The primary uses of benzene are as an additive in gasoline, chemical manufacturing and solvent operations with chemical processing being the major use. While benzene is used in the commercial production of literally hundreds of compounds (4), its major uses are as the starting material for styrene (45%), cumene/phenol (20%) and cyclohexane (17%) (2). These compounds, in turn, are used in production of polystyrene plastics and rubbers and other fabricated plastic products.

Benzene is wide-spread in the environment, both in the air and water. While the levels of environmental exposure are significantly less than the industrial levels, there is no proof than these levels are inconsequential.

The health effects of benzene have been extensively reviewed recently (5), especially with respect to its potential carcinogenic effects. Even with the recognition of benzene toxicity for over 50 years much of its action is still poorly understood. The most serious effect of chronic exposure is depression of the hematopoietic system ranging from milk reversible depression of some of the formed elements to aplastic anemia and leukemia. The latter has been particularly difficult to study since no animal model has been found in which benzene induces leukemia dispite epidemiological evidence linking the two in humans. Other toxic effects of benzene are central nervous system depression and histochemical changes in kidney, liver, small intestine, spinal cord and heart (6).

In view of these serious consequences from chronic benzene exposure, an evaluation of the exposure/body burden of benzene in the general human population in areas of relatively high (industrial and urban), medium (urban) and low (rural) benzene emissions is to be undertaken.

2. Description of the Survey Plan

This project is an epidemiologic study of exposure and absorption of benzene among populations potentially exposed to benzene from urban environments, manufacturing or industrial users, or industrial storage facilities. At each of two performance sites, a panel of respondents will be selected and recruited; this panel will represent varying distances from emission sources. A questionnaire will be administered for each individual selected for the study to obtain information on demographic variables, residence histories, and potential special exposure situations. For each individual, a sample of exposure (using a small personal monitoring device) and breath (representing absorption or body burden) will be collected; tap water samples will be collected at each residence. Samples (air, breath, and water) will be analyzed for benzene by gas chromatography/flame ionization detection.

Two locations, St. Louis, MO, and Houston, TX have been chosen as performance sites based on exposure and emisson information (7). Subject selection will be by stratified area sampling; three areas at each site will be geographically designated as high, medium, and low exposure area, on the basis of emission sources and wind patterns. To compensate for meteorological variability, the areas will radiate in all directions from the emission sources. The exact boundaries of the target areas are subject to local condition data which will be obtained by site visits of the person responsible for drawing the sampling frame. Since some of the low exposure areas will be suburban and rural, census data may not be available for the total target population. The combined total target population in the St. Louis and Houston areas is 1,857,377; from this target population, a total of 150 persons will be recruited.

Delineation of exposure area boundaries will use dispersion modeling and other mapping techniques. Within each exposure area, sublevels will be established based on city blocks and other physical features. Household interviewers will be assigned specific segments to canvass and a specific order in which to do the canvassing. Persons contacted and meeting eligibility requirements will be asked to participate. This process will continue until either all segments have been exhausted or the target population has been achieved. A record of all household contacts will be made; nonrespondents (those not able to be contacted) and nonparticipants (refusals) will be recorded for each interviewer and at each site. These records will be compared to determine the likely effect of any bias in the final results. To try to reduce the nonparticipation rate, and to reimburse the subject for time spent on the study, volunteers will be offered a $5.00 incentive for participating.

Approximately 75 persons, evenly divided among the three (high, medium, and low) exposure areas, will be selected at each site. In order to participate in the study, an individual must meet certain criteria; potential participants must reside in the target areas during the data collection period, be 25-50 years of age, and be at their place of residence during the time that exposure is monitored. In addition, potential participants will be carefully screened to eliminate individuals who smoke, suffer respiratory distress, take prescription medications on a regular daily basis, and who experience occupational or avocational exposure.

The agency statistician who has reviewed this work plan and who has been involved from the selection of the contractor is:

David Svendsgaard
Office of Statistics and Data Management
Health Effects Research Laboratory
Research Triangle Park, NC 27711
FTS 625-2468

The contractor for this study is:

Research Triangle Institute
P. O. Box 12194
Research Triangle Park, NC 27709

The contractor is responsible for all phases of the study, including study design, subject recruitment, chemical analysis of all samples, human surveying and the statistical analysis and report writing. RTI promises to ensure the confidentiality of all personal data collected under this contract. The only place a person's name and his study number will appear together is on the consent form which will not be converted to machine-readable form and will be sored in a secure area. All material will be entered into the computer by study identification number. All publications resulting from this project will use statistical compilations of data. No individual names and associated data will be released.

The contractor is presently testing and refining procedures for measuring benzene exposure and absorption. The data collection instruments are modifications of questionnaires which were used in another EPA-sponsored research effort (OMB No. 158-S77006) which have been administered to some 1,115 respondents; the data collection instruments for the benzene study are more conside, efficient, and relevant, having profited from the earlier study.

3. Tabulation and Publication Plans

The results of the project will be summarized in a final report from the contractor to EPA. A draft of this report should be available approximately 9 months after approval of the questionnaire.

In the analysis, RTI will examine the following relationships:

a. Analysis of the relationship between the levels of benzene in humans as measured by breath samples and various levels of exposure to benzene (e.g., low, moderate, and high or urban and rural).

b. Analysis of the relationship between the levels of benzene in human breath samples and environmental levels of benzene (i.e., levels in air, water, and possibly food).

The principal statistical techniques that will be used to examine these relationships are the analysis of variance and multiple regression. In some instances, it may be worthwhile to employ the technique of stepwise regression; this technique can be used to give insight into the relative strengths of the various demographic and environmental variables in predicting toxic body burdens in humans. In addition to using these three techniques, other techniques which will be employed to examine the relationships of interest include computing correlations between pairs of variables; examining scatter plots of body burden level versus benzene exposure levels and environmental and demographic variables; and computing means of the environmental and demographic variables for various body burden levels and then plotting these means.

4. Time Schedule for Data Collection and Publication

Within six weeks of approval of the study RTI will be in the field at the first study site. Assuming a May approval date, data collection could begin in June. Five months will be required for data collection. To complete all analytic work and produce the draft report will take three months after this.

5. Consultations Outside the Agency

Dr. Frank Johnson
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Dr. John M. Harrelson
Assistant Professor of Orthopedic Surgery and Pathology
Duke University Medical Center
Durham, NC

Dr. Stephen H. Gehlbach
Adjunct Assistant Professor of Epidemiology
School of Public Health
University of North Carolina
Chapel Hill, NC

and

Assistant Professor, Department of Community Health Sciences
Duke University Medical Center
Durham, NC

6. Estimation of Respondent Reporting Burden

The burden of this project on respondents covers: the time necessary to complete the questionnaire; the time and inconvenience of allowing the field interviewer into the household to collect the tap water samples; and the time and inconvenience of providing the breath and exposure samples. All efforts will be undertaken to reduce to a minimum respondent burden, but in order to complete all household data collection, approximately one hour of time may be required of the participant, including the collection of all relevant samples. More specifically, we anticipate that up to 30 minutes may be required to complete the questionnaires for a participant, 15 minutes will be required to collect the tap water sample and explain the exposure monitor, and 15 minutes will be required to obtain the breath sample.

7. Sensitive Questions

None of the questions is considered to be particularly sensitive.

8. Estimate of Cost to the Federal Government

The present estimated cost of the project is $150,000.

9. References

1. E. V. Anderson, Chem. Eng. News, 54 (19), 34 (1976).
2. Anon., Chem. Eng. News, 54, (47), 17 (1976).
3. P. H. Howard and P. R. Durkin, Sources of Contamination, Ambient Levels, and Fate of Benzene in the Environment. EPA 560/5-75-005, Dec., 1974.
4. SRI, Chemical Origins and Markets, Stanford Research Institute, Menlo Park, CA, 1967, p. 18-19.
5. Benzene Health Effects Assessment, U. S. Environmental Protection Agency, External Review Draft, October 1977.
6. J. J. Kocsis and R. Songder, "Current Concepts of Benzene Toxicity", CRC Crit. Rev. Toxicol., 3, 265 (1975).
7. S. J. Mara and S. S. Lee, Human Exposures to Atmospheric Benzene, EPA Contract 68-01-4314, Final Report, October, 1977.

APPENDIX E

DATA LISTING OF AIR AND BREATH BENZENE LEVEL DISTRIBUTIONS BY SITE AND BY EXPOSURE STRATA

Table E-1. AIR AND BREATH BENZENE LEVELS AND SAMPLE WEIGHTS FOR HOUSTON AND ST. LOUIS

OBS	Site	Exposed1/	Air2/	Breath	Weight3/	Stratum	SEG2
1	HOUSTON	HIGH	16.0	3.1	27.0	1	11
2	HOUSTON	HIGH	32.0	0.0	27.0	1	11
3	HOUSTON	HIGH	5.2	1.7	27.0	1	11
4	HOUSTON	HIGH	8.6	2.8	27.0	1	11
5	HOUSTON	HIGH	.	0.8	27.0	1	11
6	HOUSTON	HIGH	31.0	5.6	23.6	1	12
7	HOUSTON	HIGH	14.0	8.6	23.6	1	12
8	HOUSTON	HIGH	14.0	5.1	23.6	1	12
9	HOUSTON	HIGH	13.0	3.0	23.6	1	12
10	HOUSTON	HIGH	35.0	0.0	29.0	1	19
11	HOUSTON	HIGH	6.1	3.5	27.0	2	15
12	HOUSTON	HIGH	11.0	.	27.0	2	15
13	HOUSTON	HIGH	6.7	0.0	25.4	2	17
14	HOUSTON	HIGH	3.1	14.0	25.4	2	17
15	HOUSTON	HIGH	6.7	1.4	25.4	2	17
16	HOUSTON	HIGH	18.0	3.5	25.4	2	17
17	HOUSTON	MEDIUM	10.0	1.3	10260.0	1	26
18	HOUSTON	MEDIUM	10.0	1.0	10260.0	1	26
19	HOUSTON	MEDIUM	8.0	.	6080.0	1	27
20	HOUSTON	MEDIUM	2.0	2.0	6080.0	1	27
21	HOUSTON	MEDIUM	7.0	1.0	6080.0	1	27
22	HOUSTON	MEDIUM	65.0	4.1	22775.0	1	29
23	HOUSTON	MEDIUM	11.0	2.0	4556.0	2	24
24	HOUSTON	MEDIUM	4.4	2.7	4556.0	2	24
25	HOUSTON	MEDIUM	12.0	4.8	7973.0	2	25
26	HOUSTON	MEDIUM	3.1	3.0	7973.0	2	25
27	HOUSTON	MEDIUM	33.0	2.4	11387.5	3	20
28	HOUSTON	MEDIUM	26.0	2.5	8350.8	3	21
29	HOUSTON	MEDIUM	4.6	2.3	8350.8	3	21
30	HOUSTON	MEDIUM	11.0	2.0	8350.8	3	21
31	HOUSTON	MEDIUM	45.0	1.0	6825.0	4	22
32	HOUSTON	MEDIUM	10.0	.	6825.0	4	22
33	HOUSTON	MEDIUM	20.0	1.8	6825.0	4	22
34	HOUSTON	MEDIUM	25.0	4.4	13650.0	4	23
35	HOUSTON	LOW	9.8	.	5518.3	1	33
36	HOUSTON	LOW	4.3	.	5518.3	1	33
37	HOUSTON	LOW	18.0	7.5	5518.3	1	33
38	HOUSTON	LOW	10.0	4.4	5518.3	1	33
39	HOUSTON	LOW	13.0	.	3110.8	1	37
40	HOUSTON	LOW	17.0	0.0	394.0	2	34
41	HOUSTON	LOW	3.4	2.9	2482.2	2	36
42	HOUSTON	LOW	4.5	.	2482.2	2	36
43	HOUSTON	LOW	21.0	0.3	2077.5	3	30
44	HOUSTON	LOW	4.0	2.0	2077.5	3	30
45	HOUSTON	LOW	18.0	1.4	2079.0	3	32
46	HOUSTON	LOW	17.0	0.7	2079.0	3	32
47	HOUSTON	LOW	9.0	1.7	2079.0	3	32
48	HOUSTON	LOW	13.0	1.9	2079.0	3	32
49	HOUSTON	LOW	27.0	4.0	2079.0	3	32
50	HOUSTON	LOW	5.6	8.2	8334.1	3	35
51	ST LOUIS	HIGH	17.0	9.2	10.8	1	31
52	ST LOUIS	HIGH	25.0	4.6	10.8	1	31
53	ST LOUIS	HIGH	86.0	9.2	10.8	1	31
54	ST LOUIS	HIGH	86.0	16.0	10.8	1	31
55	ST LOUIS	HIGH	17.0	4.2	10.8	1	31
56	ST LOUIS	HIGH	14.0	3.5	9.0	1	32

Table E-1 (cont'd.)

OBS	SITE	EXPOSED	AIR	BREATH	WEIGHT	STRATUM	SEG2
57	ST LOUIS	HIGH	.	7.3	9.00	1	32
58	ST LOUIS	HIGH	17.0	7.7	9.00	1	32
59	ST LOUIS	HIGH	6.2	8.9	6.67	1	35
60	ST LOUIS	HIGH	23.0	3.8	6.67	1	35
61	ST LOUIS	HIGH	11.0	1.6	6.67	1	35
62	ST LOUIS	HIGH	52.0	7.7	6.67	1	35
63	ST LOUIS	HIGH	11.0	3.0	6.67	1	35
64	ST LOUIS	HIGH	6.2	.	6.67	1	35
65	ST LOUIS	HIGH	3.7	4.1	9.75	2	33
66	ST LOUIS	HIGH	17.0	5.7	9.75	2	33
67	ST LOUIS	HIGH	6.6	2.8	9.75	2	33
68	ST LOUIS	HIGH	25.0	4.7	9.75	2	33
69	ST LOUIS	HIGH	3.8	2.1	9.75	2	33
70	ST LOUIS	HIGH	3.8	6.5	9.75	2	33
71	ST LOUIS	HIGH	35.0	.	9.75	2	33
72	ST LOUIS	HIGH	18.0	2.5	9.75	2	34
73	ST LOUIS	HIGH	18.0	4.5	9.75	2	34
74	ST LOUIS	HIGH	.	6.2	9.75	2	34
75	ST LOUIS	HIGH	19.0	12.0	9.75	2	34
76	ST LOUIS	MEDIUM	7.4	7.0	2267.25	1	11
77	ST LOUIS	MEDIUM	.	.	2267.25	1	11
78	ST LOUIS	MEDIUM	.	19.0	1763.42	1	12
79	ST LOUIS	MEDIUM	.	14.0	1763.42	1	12
80	ST LOUIS	MEDIUM	13.0	7.0	2016.00	2	13
81	ST LOUIS	MEDIUM	4.0	.	2016.00	2	13
82	ST LOUIS	MEDIUM	125.0	26.0	2016.00	2	14
83	ST LOUIS	MEDIUM	.	4.4	2016.00	2	14
84	ST LOUIS	MEDIUM	3.5	11.0	1602.32	3	15
85	ST LOUIS	MEDIUM	5.1	9.4	1602.32	3	15
86	ST LOUIS	MEDIUM	.	2.3	1602.32	3	15
87	ST LOUIS	MEDIUM	.	3.1	1602.32	3	15
88	ST LOUIS	MEDIUM	47.0	.	1583.47	3	16
89	ST LOUIS	MEDIUM	18.0	3.8	1583.47	3	16
90	ST LOUIS	MEDIUM	20.0	2.3	1583.47	3	16
91	ST LOUIS	MEDIUM	.	.	1583.47	3	16
92	ST LOUIS	MEDIUM	10.0	.	1583.47	3	16
93	ST LOUIS	MEDIUM	22.0	4.0	1583.47	3	16
94	ST LOUIS	MEDIUM	.	9.4	1583.47	3	16
95	ST LOUIS	MEDIUM	19.0	7.0	1583.47	3	16
96	ST LOUIS	LOW	32.0	11.0	282.86	1	21
97	ST LOUIS	LOW	17.0	1.1	282.86	1	21
98	ST LOUIS	LOW	22.0	2.2	282.86	1	21
99	ST LOUIS	LOW	.	5.5	282.86	1	21
100	ST LOUIS	LOW	9.1	6.2	282.86	1	21
101	ST LOUIS	LOW	46.0	4.9	664.71	1	23
102	ST LOUIS	LOW	44.0	.	664.71	1	23
103	ST LOUIS	LOW	30.0	11.0	664.71	1	23
104	ST LOUIS	LOW	.	.	664.71	1	23
105	ST LOUIS	LOW	.	1.4	664.71	1	23
106	ST LOUIS	LOW	30.0	.	664.71	1	23
107	ST LOUIS	LOW	10.0	.	664.71	1	23
108	ST LOUIS	LOW	118.0	8.8	413.60	1	24
109	ST LOUIS	LOW	4.2	17.0	413.60	1	24
110	ST LOUIS	LOW	4.2	5.0	413.60	1	24
111	ST LOUIS	LOW	3.4	.	413.60	1	24
112	ST LOUIS	LOW	.	9.3	413.60	1	24

Table E-1 (cont'd.)

OBS	SITE	EXPUSED	AIR	BREATH	WEIGHT	STRATUM	SEG2
113	ST LOUIS	LUW	.	6.1	413,600	1	24
114	ST LOUIS	LUW	9.0	5.1	520,000	2	25
115	ST LOUIS	LUW	43.0	.	520,000	2	25
116	ST LOUIS	LUW	3.9	2.6	297,143	2	26
117	ST LOUIS	LUW	3.9	5.2	297,143	2	26
118	ST LOUIS	LUW	6.3	18.0	297,143	2	26

1/ Sampling strata exposure level = high, medium or low

2/ Air, breath = ug/m^3

3/ Sampling weight used to weight benzene air and breath levels so that area estimates could be made.

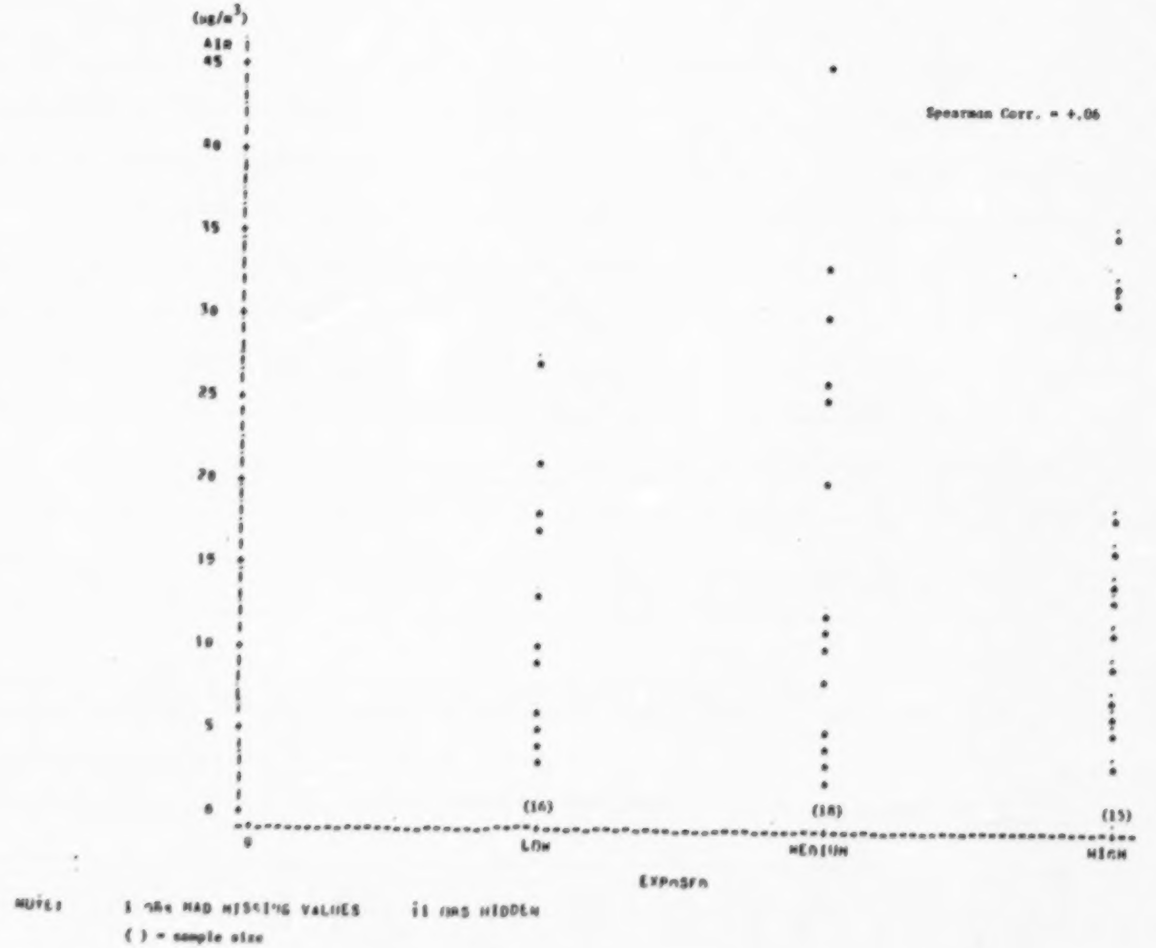
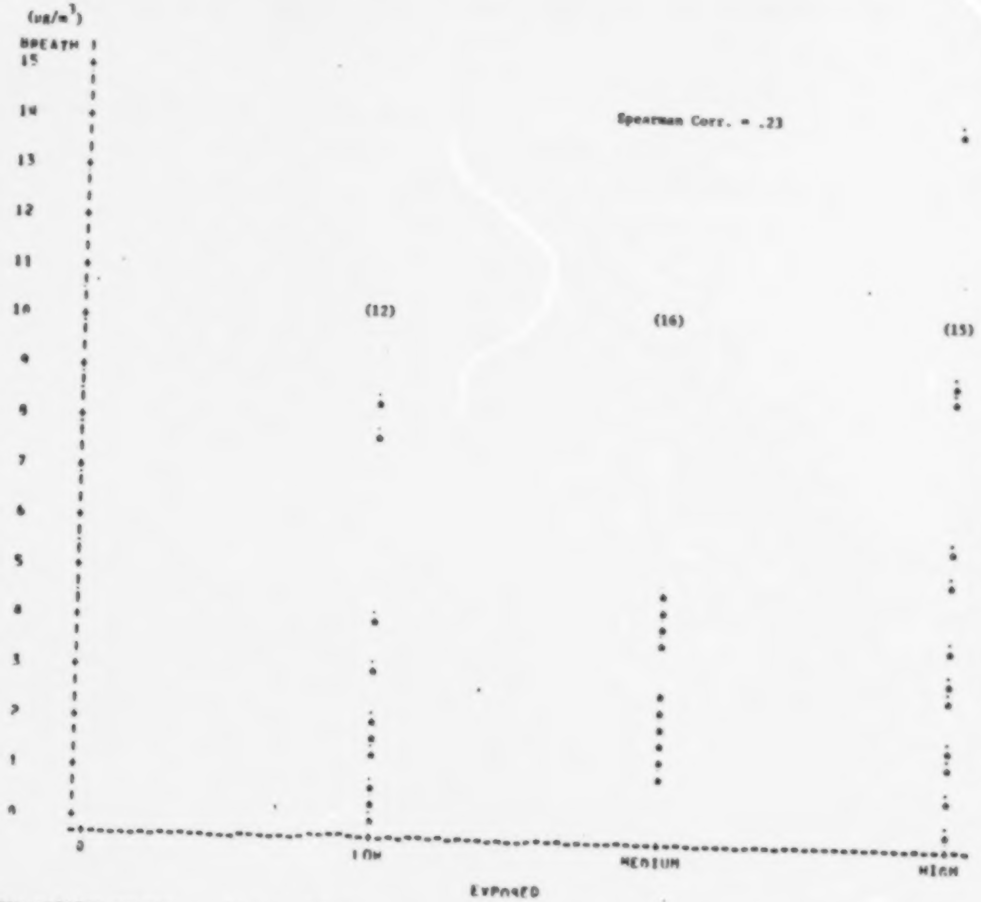
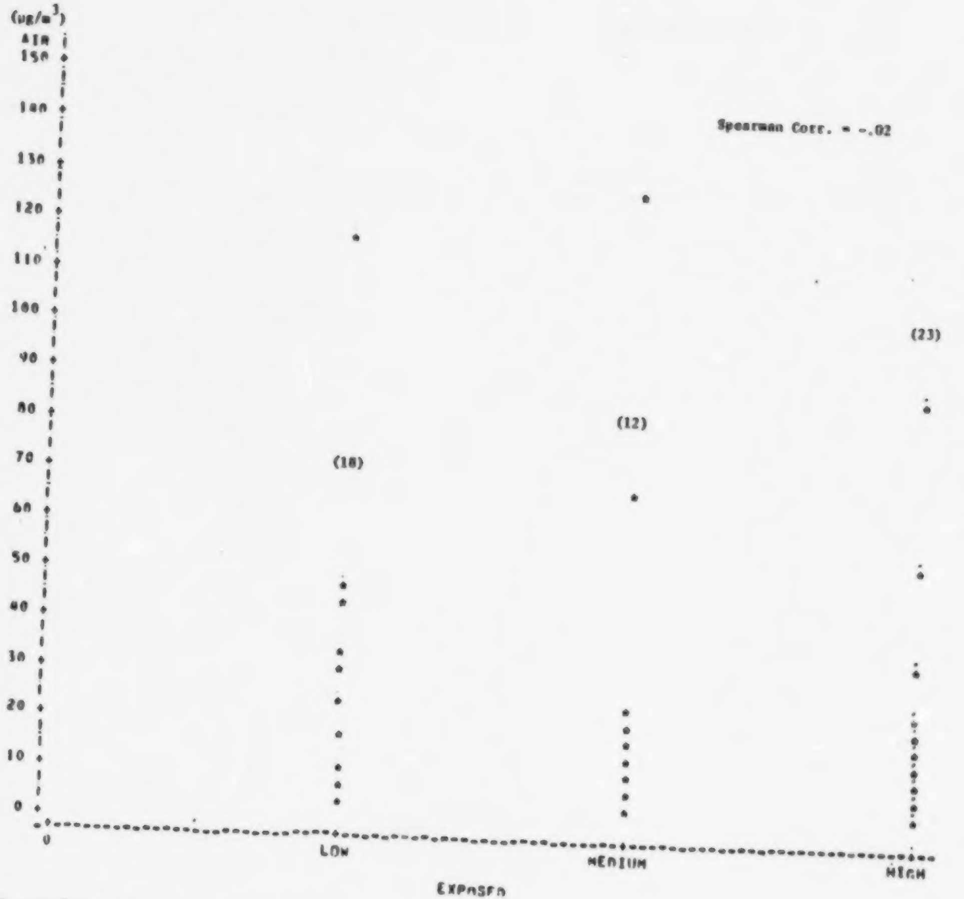


Figure E-1. Site = Houston. Plot of Air Exposed = *.



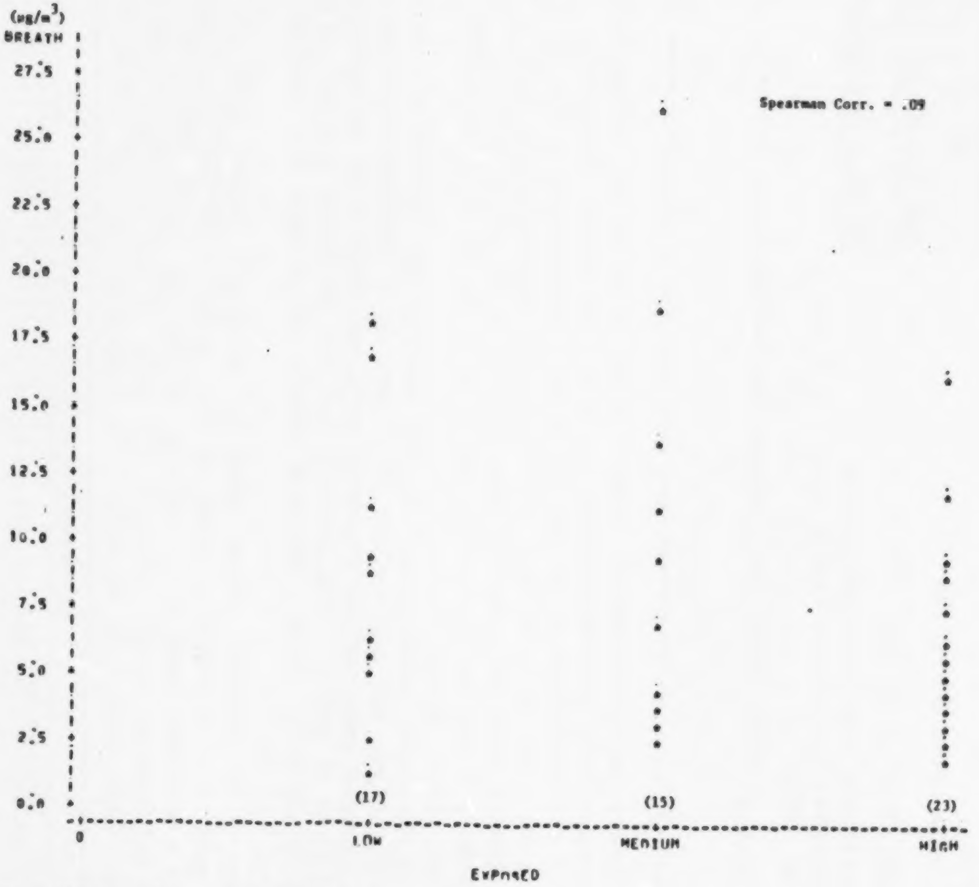
NOTE: 7 OBS HAD MISSING VALUES 11 OBS HIDDEN
( ) = sample size

Figure E-2. Site = Houston. Plot of breath exposed = *.



NOTE: 15 OBS HAD MISSING VALUES 24 OBS HIDDEN
( ) sample size

Figure E-3. Site = St. Louis. Plot of air exposed = *.



NOTE: 13 OBS HAD MISSING VALUES 22 OBS HIDDEN

( ) sample size

Figure E-4. Site = St. Louis. Plot of breath exposed = *.